APPENDIX A

Example 1.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of infulenza (A, B, and mixed) and accute viral respiratory infections (AVRI) in children was studied at the Research Institute of Influenza of the Russian Academy of Medical Sciences. The subjects of the double blinded placebo controlled trial were children of both genders 1 to 10 years old who had been diagnosed with influenza or AVRI as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=120) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=166) in combination with the symptomatic therapy during 7-14 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced the overall duration of the disease (from 7.5±0.28 to 5.8±0.24 days) and the duration of the main symptoms of the disease, such as fever (from 4.0±0.13 to 2.4±0.13 days), intoxication symptoms (on the average by 1.5 days) and catarrh symptoms (by 1.7 days). No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of the influenza virus and AVRI in children have thus been shown.

Example 2

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of AVRI complicated by stenosing laryngotracheobronchitis bronchitis in children was studied at the Russian State Medical University. The subjects of the double blinded placebo controlled trial were children of both genders 6 months to 14 years old who had been diagnosed with AVRI and stenosing laryngotracheobronchitisas as confirmed by the laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=50) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=50) in combination with the symptomatic therapy during 5-7 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

It has been shown that the ultra-low doses of polyclonal antibodies to human interferon gamma led to a clinically and statistically significant reduction, as compared to a placebo, of the duration of the main symptoms of AVRI (by the factor of 1.5-2) and the duration of stenosing laryngotracheobronchitis (after three days of the therapy the number of children with the symptoms of laryngitis was reduced by more than a factor of 7). No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of AVRI accompanied by stenosing laryngotracheobronchitis in children, including the cases of the mixed viral and bacterial infections, have thus been shown.

Example 3

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of AVRI in children was studied at the Volgograd State Medical University, Volgograd, Russia. The subjects of the comparison trial were children of both genders 4 to 7 years old who had been diagnosed with AVRI as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=60) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or immunal (n=60, 45 drops/day) or arbidol (n=40, 150-300 mg/day) in combination with the symptomatic therapy during 7-10 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced, as compared to the comparison treatment, the duration of fever (on the average by 0.5-1.3 days), headaches (0.6-0.9 days), adynamia (0.7-1.2 days), pharyngeal hypermia (1.9-2.7 days), and rhinitis (2.0-2.9 days). No undesirable effects were registered upon administration of the preparation.

The above study has shown that the use of the ultra-low doses of the antibodies in the treatment of AVRI and influenza in children is superior in efficacy to immunal and is comparable with arbidol.

Example 4.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of infulenza (A, B, and mixed) and AVRI in children was studied at the Bashkir State Medical University, Ufa. The subjects of an open trial without comparison were children of both genders 1 to 6 years old who had been diagnosed with influenza or AVRI as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=30) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon). The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The study has shown that already after 1 day of treatment with ultra-low doses of the polyclonal antibodies to human interferon gamma the percentage of children with febril fever (body temperature over 38.6°C) was reduced from 56.7% to 20%. After 2 days of the therapy normal body temperature was registered in 50% of the children. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of the influenza virus and AVRI in children have thus been shown.

Example 5.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of varicella (chickenpox) in children was studied at the Volsk Children's Hospital, Volsk, Russia. The subjects of the double blinded placebo controlled trial were

children of both genders 1 to 18 years old who had been diagnosed with varicella as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=136) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=100) in combination with the symptomatic therapy during a maximum of 10 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control group showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced the duration of the main symptoms of the disease and the frequency of complications. For example, the duration of fever was reduced on the average from 4.3±0.1 to 1.4±0.1 days, the period of new rash appearance was reduced from 5.7±0.1 to 1.7±0.1 days, itching from 5.8±0.1 to 1.5±0.1 days. The percentage of children with pustules was reduced from 96% to 14.7% and the percentage of children who needed an additional anitbacterial therapy – from 20% to 2.2% No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of varicella in children have thus been shown.

Example 6.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of infectious mononucleosis in children was studied at the Siberian State Medical University, Tomsk, Russia. The subjects of the double blinded placebo controlled trial were children of both genders 3 to 12 years old who had been diagnosed with infectious mononucleosis as confirmed by laboratory tests. The subjects entered the study 3-7 days after the onset of the disease. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=30) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=30) in combination with the symptomatic therapy during a maximum of 14 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The study showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the duration of angina from 3.6±0.4 to 2.7±0.3 days. The lymphoproliferative syndrome was reduced as follows: lymph adenopathy remained for 13.0±0.6 days within the placebo group and for 8.1±0.7 in the main group; hepatomegaly remained for 11.4±0.8 and 7.1±0.8 days, respectively. No late-stage bacterial complications were registered (within two weeks following the termination of the treatment) in the group of patients who received ultra-low doses of the antibodies to human interferon gamma, whereas 23.3% of patients in the placebo group developed such late complications. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of the infectious mononucleosis and prevention of bacterial complications in children have thus been shown.

Example 7.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of AVRI with intestinal syndrome and coronaviral infection (ACI) in children was studied at the Research Institute of Influenza of the Russian Academy of Medical Sciences. The subjects of the double blinded placebo controlled trial were children of both genders 1 to 10 years old whose diagnosis had been by the laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=100) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=50) in combination with the symptomatic therapy during 7-14 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma led to a statistically significant reduction of the overall duration of fever (2.18±0.08 and 3.49±0.22 for AVRI+ACI; 2.05±0.10 and 3.38±0.37 for CVI), reduced duration of the intoxication symptoms (2.70±0.11 and 4.28±0.27 for AVRI+ACI; 2.36±0.15 and 4.80±0.37 for CVI), catarrh symptoms in the nasopharynx (4.48±0.14 and 6.74±0.31 for AVRI+ACI; 4.05±0.17 and 6.68±0.37 for CVI), and gastrointestinal symptoms (3.30±0.16 and 4.62±0.38 for AVRI+ACI; 3.07±0.23 and 5.13±0.57 for CVI), respectively. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of AVRI with intestinal syndrome and coronaviral infection in children have thus been shown.

Example 8.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of accute intestinal viral infection caused by caliciviruses in children was studied at the Research Institute of Child Infections, Saint-Petersburg, Russia. The subjects of the placebo controlled trial were children of both genders 6 months to 15 years old who had been diagnosed with caliciviral infection as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=30) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=30) in combination with the symptomatic therapy during 5-7 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the duration of the main symptoms of the disease, such as fever (from 2.9±0.3 to 1.3±0.2 days), vomiting (from 2.4±0.2 to 1.5±0.2 days) and diarrhea (from 2.8±0.2 to 1.2±0.1 days). It was also shown that the preparation reduced viral shedding: by the end of the treatment the percentage of children with the virus shedding was reduced from 53% in the conrol group to 3%. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of accute intestinal viral infection caused by caliciviruses in children have thus been shown.

Example 9

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of accute intestinal viral infection caused by rotaviruses in children was studied at the Rostov State Medical University, Rostov-on-Don, Russia. The subjects of the placebo controlled trial were children of both genders 1.5 to 5.5 years old who had been diagnosed with rotaviral infection as confirmed by laboratory tests. The subjects entered the study 1-2 days after the onset of the disease. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=17) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) in combination with a standard therapy (sorbents, enzymes, probiotics, rehydration, antibiotics) whereas the children in the control group (n=18) only received the standard therapy. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control group showed that the addition of ultra-low doses of the polyclonal antibodies to human interferon gamma to the standard therapy led to a statistically significant reduction of the duration of all symptoms of the disease, such as duration of fever (from 4.9±0.3 to 3.4±0.2 days), diarrheal syndrom (from 5.9±0.34 to 3.6±0.2 days), and vomiting (from 1.7±0.13 to 1.1±0.1 days). No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the combined treatment of rotaviral gastroenteritis in children have thus been shown.

Example 10.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of respiratory syncytial virus in children was studied at the Research Institute of Influenza of the Russian Academy of Medical Sciences. The subjects of the double blinded placebo controlled trial were children of both genders 1 to 10 years old whose diagnosis had been confirmed by the laboratory tests. The subjects entered the study 1-2 days after the onset of the disease with the body temperature 37.5°C or above. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=40) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=36) in combination with the symptomatic therapy during 7-14 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the overall duration of the main clinical symptoms, such as fever (on the average, by 1.2 days), intoxication (by 1 day), catarrh symptoms (by 2.1 days), and the duration of inpatient care (by 2 days). No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of infections caused by respiratory syncytial virus have thus been shown.

Example 11.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children was studied at the Research Institute of Influenza of the Russian Academy of Medical Sciences. The subjects of the double blinded placebo controlled trial were children of both genders 1 to 10 years old. The children (n=103) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=101) during 3 months. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The above study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma led to a statistically significant reduction of the frequency of both sporadic and the group AVRI. For example, the frequency of the group outbreaks was reduced from 8 to 3, as compared to the placebo group. The mean number of AVRI cases per child was 1.19 in the main group and 2.39 in the control group. The overall index of epidemic effectiveness (IEE) was 2.02 and the coefficient of epidemic effectiveness (CEE) was 50.05. The administration of the claimed preparation also resulted in a reduced infection in children: the frequency of the virus shedding was reduced by a factor of 2.1. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children have thus been shown.

Example 12.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children with frequent infections was studied at the Russian State Medical University, Moscow, Russia. The subjects of the double blinded placebo controlled trial were children of both genders 6 months to 3 years old. The children (n=100) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=100) during 1 or 3 months. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI by a factor of 2.3 and reduced the frequency of moderately severe AVRI cases accompanied by conjunctivitis or stomatitis. The frequency of the most common complications of AVRI, such as mucous purulent rhinitis, was reduced by a factor of 2 upon prophylactic administration of the claimed preparation. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children with frequent infections have thus been shown.

Example 13.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of AVRI in children with bronchial asthma of intermittent and moderate severity was studied at the Siberian State Medical University, Tomsk, Russia. The subjects of the single blinded placebo controlled trial with an additional open comparison group were children of both genders 1.5 to 7 years old. The children (n=40) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=26) during 3 months. The children in the comparison group (n=33) were once vaccinated by Grippol in the beginning of the trial (IM, 0.5 ml). The children were evaluated for the incidence and duration of AVRI and for exacerbations of bronchial asthma.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma and Grippol reduced the incidence of AVRI and the frequency of complications of bronchial asthma. For example, the percentage of children who did not acquire AVRI was 50% in the main group, 51.5% in the Grippol group and 19% in the placebo group. The duration of AVRI was 2.6 and 2.2 times lower than in the placebo group, respectively. The percentage of children with no exacerbations of bronchial asthma was 65% in the group receiving the claimed preparation, 78.8% in the group vaccinated by Grippol, and 23.1% in the placebo group. The average duration of the exacerbations of bronchial asthma was twice as short in the main group as in the groups vaccinated by Grippol or receiving placebo. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children with bronchial asthma have thus been shown.

Example 14.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of AVRI in children was studied at the Volgograd State Medical University, Volgograd, Russia. The subjects of the comparison trial were children of both genders 3 to 7 years old. The children (n=30) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=60) during 3 months. The children in the comparison group (n=30) received IRS-19 (1 dose two times a day for 2 weeks; 2 doses 2-5 times a day upon appearance of the AVRI symptoms); 30 patients received combined therapy with the claimed preparation and IRS-19. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The above study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence AVRI when used as the prophylactics both alone, and in the combination with IRS-19. For example, the percentage of children that acquired AVRI during the prophylactic treatment was 16.7% in the main group, 20.0% in the IRS-19 group, and 13.3% in the group that received the combinatation of the claimed preparation with IRS-19. The percentage of children that acquired the disease in the placebo group was 45%, out of which 5% aquired it twice. No undesirable effects were registered upon administration of the preparation.

The above study demonstrated efficacy and safety of the claimed preparation in the prophylactics of AVRI in children when used both alone and in combination with other means of AVRI prophylactics.

Example 15.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of AVRI in children with HIV infection, perinatal contact in the HIV infection, was studied at the Saint-Petersburg State Pediatric Medical Academy, Saint-Petersburg, Russia. The subjects of the trial were children of both genders 4 months to 3 years old. The children (n=45) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=100) during 3 months. The comparison group included 105 patients. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The comparison with the control group showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI from 100% to 73.3%. The repeated cases of ARVI were registered less frequently in the group receiving the claimed preparation (20% vs 40% in the control group). Added bacterial infections were registered in 26.2% of children receiving the claimed preparation as compared to 37.8% in the control group.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children with HIV infection, perinatal contact in the HIV infection have thus been shown.

Example 16.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the urgent prophylactics of tick-borne encephalitis in children was studied at the Research Institute of Child Infections, Saint-Petersburg, Russia. The subjects of the trial were children of both genders 2 to 17 years old. The children (n=82) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day) (children's anaferon). The comparison group included 321 patients injected with anti-tick immunoglobulin. The children were evaluated for the incidence of tick-borne encephalitis and the number of children with the antigen of tick-borne encephalitis virus (as determined by the PCR).

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma prevented the development of tick-borne encephalitis in 100% of patients, whereas 15.3% of children in the comparison group developed the disease. The antigen of the tick-borne encephalitis virus was detected in a single case (1.2%) in the main group and in 44% of patients in the comparison group.

The efficacy and safety of the claimed preparation in the urgent prophylactics of tick-borne encephalitis in children have thus been shown.

Example 17.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of accute respiratory diseases (ARD) in children was studied at Nurseries No 603 and 2095, Moscow, Russia. The subjects of the comparison trial were children of both genders 2 to 7 years old. The children (n=48) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3 pills/day upon appearance of ARD symptoms) (children's anaferon) or a comparison treatment (Sandra) (n=49) during 40 days. The children were evaluated for the incidence of ARD and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of ARD by a factor of 1.5 as compared to the comparison treatment. The frequency of complications of ARD, such as otitis, laringotracheitis and antritis, among others, was reduced by a factor of 2 upon prophylactic administration of the claimed preparation. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of ARD in children have thus been shown.

Example 18.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children with frequent diseases was studied at the Samara State Medical University, Samara, Russia. The subjects of the placebo controlled trial were children of both genders 3 to 5 years old. The children (n=160) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=16) during 3 months. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI by a factor of 2 and reduced the frequency of moderately severe AVRI cases. The duration of the AVRI symptoms was reduced by 3 days as compared to the control group. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children with frequent diseases have thus been shown.

Example 19.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children was studied at the Russian State Medical University, Moscow, Russia. The subjects of the placebo controlled trial were children of both genders 7 to 8 years old. The children (n=100) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms)

(children's anaferon) or placebo (n=100) during 40 days. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI by a factor of 3 and reduced the frequency of moderately severe AVRI cases. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children have thus been shown.

Example 20.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children was studied at the Volsk Children's Hospital, Volsk, Russia. The subjects of the placebo controlled trial were children of both genders. The children (n=148) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon) or placebo (n=136) during 2-3 months. The children were evaluated for the incidence of AVRI and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI by a factor of 1.6 and reduced the frequency of moderately severe AVRI cases. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of AVRI in children have thus been shown.

Example 21.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of accute respiratory diseases (ARD) in children with frequent diseases was studied at N.N. Burdenko Voronezh State Medical Academy, Voronezh, Russia. The subjects of the comparison trial were children of both genders 4 to 6 years old with frequent diseases. The children (n=20) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3 pills/day upon appearance of ARD symptoms) (children's anaferon) during 1 month. The control group included 20 children. The children were evaluated for the incidence of ARD and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of ARD by a factor of 2 as compared to the control group. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of ARD in children with frequent diseases have thus been shown.

Example 22.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics and treatment of AVRI in children with frequent diseases on the background of lympholaringeal ring pathology was studied at the Kemerovo State Medical Academy, Kemerovo, Russia. The subjects of the placebo controlled trial were children of both genders 2 to 4 years old with frequent diseases. The children (n=33) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3 pills/day upon appearance of ARD symptoms) (children's anaferon) or placebo (n=20) during 3 months. The control group included 20 children. The children were evaluated for the incidence of ARD and, in the case of the disease development, for the duration and severity of the disease and for the risk of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of ARD by a factor of 2.5 as compared to the control group and reduced the frequency of moderately severe ARD cases. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics and treatment of ARD in children with frequent diseases on the background of lympholaringeal ring pathology have thus been shown.

Example 23.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of AVRI in children was studied at the Saratov State Medical University, Saratov, Russia. The subjects of the trial were children of both genders 1 to 5 years old who had been diagnosed with AVRI. The subjects entered the study 1-2 days after the onset of the disease (or 4-5 days in the cases of complicated ARVI) with the symptoms of rhinopharyngitis, laryngotracheitis and laryngeal stenosis. They had not received any immunomodulating or antiviral therapies before the beginning of the trial. The children (n=50) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-5 pills/day) (children's anaferon) or placebo (n=47) in combination with the symptomatic therapy. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with placebo showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced the duration of fever and other intoxication symptoms, such as adynamia and reduced appetite, on the average by 1.5 days and the cases of rhinitis by a factor of 1.6. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of AVRI in children have thus been shown.

Example 24.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of the exacerbations of bronchial asthma caused by respiratory infections in children was studied at the Novosibirsk State Medical University, Novosibirsk, Russia. The subjects of the trial were children of both genders 1 to 5 years old. The children (n=40) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics and 3-7 pills/day upon appearance of AVRI symptoms) (children's anaferon). The control group included 36 children. The children were evaluated for the frequency and duration of AVRI and the exacerbations of bronchial asthma.

The comparison with the control showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI and the frequency of exacerbations of bronchial asthma. For example, the nujber of children that had not acquired AVRI increased 2-fold (from 41.7% to 82.5%) as compared to the control. The duration of AVRI was lower by a factor of 1.9, respectively. 71% of children who had received the claimed preparation did not develop any exacerbations of bronchial asthma, whereas the corresponding percentage in the control group was 14.3%. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics of the exacerbation of bronchial asthma caused by respiratory infections in children have thus been shown.

Example 25.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of AVRI in children with allergic diseases (bronchial asthma and atopical dermatitis) was studied at the Scientific Center of Children's Health, Moscow, Russia. The subjects of the trial were children of both genders 2 to 6 years old. The children (n=34) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day in the case of prophylactics) (children's anaferon) during 3 months. The control group included 22 children. The children were evaluated for the frequency and duration of AVRI and the exacerbations of bronchial asthma.

The comparison with the control showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the incidence of AVRI and the frequency of exacerbations of bronchial asthma. For example, the number of children that had not acquired AVRI increased by a factor of 1.8 as compared to the control. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics of AVRI in children with allergic diseases (bronchial asthma and atopical dermatitis) have thus been shown.

Example 26.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of ARD in children with cardiac pathology was studied at the Bashkir State Medical University, Ufa, Russia. The subjects of the trial were children of both genders 1.5 to 7 years old. The children (n=26) received ultra-low doses of the polyclonal antibodies to human

interferon gamma (C12+C30+C50) in the form of sublingual pills (4 pill/day) (children's anaferon) in the combination with symptomatic therapy during 7-14 days. The children were evaluated for the duration of the main clinical symptoms and for the frequency and severety of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced the overall duration of the disease on the average by 3 days, the fever, intoxication symptoms and catarrth symptoms on the average by 2 days. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of ARD in children with cardiac pathology have thus been shown.

Example 27.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prophylactics of chronic recurring infections caused by the herpes virus was studied at the Samara diagnostic center, Samara, Russia. The subjects of the trial were patients of both genders 20 to 40 years old. The patients (n=30) received during the remission period ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C200) in the form of sublingual pills (1 pill/day) (anaferon) combined with the external application of Infagel (2 times daily for 10 days/month). The control group included 35 people who did not receive the claimed preparation. The patients were evaluated for the frequency and duration of the exacerbations of the disease and for the risk of complication development.

The comparison with the control showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the frequency of exacerbations in 68% of patients and reduced the duration of the exacerbations. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the prophylactics of chronic recurring infections caused by the herpes virus have thus been shown.

Example 28.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of infections caused by the herpes virus (labial herpes) was studied at the Samara State Medical University, Samara, Russia. The subjects of the trial were middle-age and young patients of both genders diagnosed with chronic recurring infections caused by the herpes virus. The patients (n=25) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C200) in the form of sublingual pills (5-8 pills/day) (anaferon) combined with acyclovir (1000 mg/day) during 5 days. The control group included 25 people who only received acyclovir. The patients were evaluated for the duration of the main clinical symptoms and for the frequency and severety of complications.

The study showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the duration of fever, intoxication symptoms and epitelization time of the herpes rash on the average by 1-2 days as compared to the control group. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in combination with specific antiviral therapy in the treatment of infections caused by the herpes virus (labial herpes) have thus been shown.

Example 29.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the prevention of recurrence in patients with ophthalmoherpes was studied at the Samara State Medical University, Samara, Russia. The subjects of the trial were middle-age and young patients of both genders diagnosed with chronic infection caused by herpes simple virus, the eyes being effected by dendritic keratitis. All patients (n=18) were treated with 1000 mg/day of valacyclovir during 10-14 days. The patients in the main group (n=10) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C200) in the form of sublingual pills (1 pill/day for 10 days – 2 times/year) (anaferon) combined with symptomatic therapy. The patients in the control group did not receive the claimed preparation. The patients were evaluated for the recurrence of the disease.

The comparison with the control group showed that ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the frequency of recurrence: only 2 out of 10 patients had recurrence of the disease. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in combination with specific antiviral therapy in the prevention of recurrence in patients with ophthalmoherpes have thus been shown.

Example 30.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of infectious mononucleosis in children was studied at the Urals Medical Academy, Yekaterinburg, Russia. The subjects of the comparison trial were children of both genders 3 to 14 years old who had been diagnosed with infectious mononucleosis as confirmed by laboratory tests. The children in the main group (n=12) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3 pills/day) (children's anaferon) in combination with acyclovir (1000 mg/day) during 7 days. The children in the comparison groups received acyclovir (1000 mg/day, n=14) or cycloferon (1250 mg/day, n=14). The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The study showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma in combination with specific therapy increased the efficacy of monotherapeutic treatment by the specific therapies. For example, the average duration of fever and angina was 2.2 days and 2.8 days in the main group, 5.1 days and 4.1 days in the acyclovir group, and 5.4 and 4.8 days in the cycloferon group, respectively. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation combined with specific antiviral therapy in the treatment of the infectious mononucleosis in children have thus been shown.

Example 31.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of viral and bacterial infections in children was studied at the Urals Medical Academy, Yekaterinburg, Russia. The subjects of the trial were children (n=242) of both genders who had been diagnosed with infectious mononucleosis or enteroviral meningitis or meningococcal meningitis as confirmed by laboratory tests. The children in the main group (n=161) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3 pills/day) (children's anaferon) in combination with basis therapy during 7 days. The children in the comparison group only received the basis therapy. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma reduced, in the case of infectious mononucleosis, the duration of fever form 5.1 to 2.2 days, angina from 4.1 to 2.8 days. In the cases of enteroviral and meningococcal meningitis, the treatment shortened the time of liquor sanation from 24 to 19 days and from 33 to 23 days, respectively. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of the viral and bacterial infections in children have thus been shown.

Example 32.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of hemorrhagic fever with renal syndrome was studied at the Bashkir State Medical University, Ufa, Russia. The subjects of the trial were children of both genders 3 to 7 years old whose diagnosis was confirmed by laboratory tests. The children in the main group (n=10) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (3-8 pills/day) (children's anaferon) in combination with symptomatic therapy. The comparison group included 20 patients. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control group showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the overall duration of the disease on the average by 3.7 days, the duration of fever by 3.3 days and the frequency of hemorrhagic syndrom development by a factor of 3. The percentage of children with renal syndrome was reduced by 15%. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of hemorrhagic fever with renal syndrome in children have thus been shown.

Example 33.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment and prevention of recurrence of tubulointerstitial nephritis was studied at the Samara State Medical University, Samara, Russia. The subjects of the trial were children of both genders 8 to 17 years old. The children in the main group (n=49) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual

pills (1 pill/day in the case of prophylactics and 3-7 pills/day in the case of treatment) (children's anaferon) in combination with symptomatic therapy. The comparison group included 22 patients. The children were evaluated for the duration of the main clinical symptoms, duration of remission and for the frequency of exacerbations.

The comparison with the control group showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the duration of the uric syndrome on the average by 4-5 days, time before the beginning of the remission by 5-6 days, and the number of exacerbations by a factor of 3. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment and prevention of recurrence of tubulointerstitial nephritis in children have thus been shown.

Example 34.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of pertussis and prevention of the pertussis complications was studied at the Saint-Petersburg State Pediatric Medical Academy, Saint-Petersburg, Russia. The subjects of the trial were children of both genders 1 month to 7 years old. The children in the main group (n=12) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1-7 pills/day) (children's anaferon). The comparison group included 25 patients. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control group showed that the administration of the ultra-low doses of the polyclonal antibodies to human interferon gamma reduced the duration of fever by 1.5 days. In the case of prophylactic treatment, the complications or pertussis in the form of AVRI were detected 1.6 times less frequently. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the treatment of pertussis and prevention of the pertussis complications in children have thus been shown.

Example 35.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the complex therapy of patients with pollinosis and atopic dermatitis accompanied by the syndrome of secondary immune deficiency was studied at the Rostov State Medical University, Rostov-on-Don, Russia. The subjects of the double blinded placebo controlled trial were children of both genders. The children in the main group (n=40) received ultra-low doses of the polyclonal antibodies to human interferon gamma (C12+C30+C50) in the form of sublingual pills (1 pill/day) (children's anaferon) or placebo (n=40) in combination with basis therapy during 2 months. The comparison group included 25 patients. The therapeutic efficacy was evaluated by the 5-point Duchaine scale in the patients with pollinosis and by the SCORAD index in the patients with atopic dermatitis.

The comparison with the control showed that ultra-low doses of the polyclonal antibodies to human interferon gamma significantly reduced the duration of AVRI episodes by 75%. The average improvements according to scales Duchaine and SCORAD were 20%. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the complex therapy of patients with pollinosis and atopic dermatitis accompanied by the syndrome of secondary immune deficiency in children have thus been shown.

Example 36.

The efficacy and safety of ultra-low doses of polyclonal antibodies to human interferon gamma in the treatment of pseudotuberculosis was studied at the Saint-Petersburg State Pediatric Medical Academy, Saint-Petersburg, Russia. The subjects of the double blinded placebo controlled trial were children of both genders 1 to 7 years old with moderately severe pseudotuberculosis. The children in the main group (n=32) received ultra-low doses of the polyclonal antibodies to human interferon gamma in the form of sublingual pills (3 pill/day) (children's anaferon) in combination with standard therapy (antibacterial, symptomatic) during 14 days. The comparison group included 144 patients. The children were evaluated for the duration of the main clinical symptoms and for the frequency and degree of complications.

The comparison with the control group showed that the inclusion of ultra-low doses of the polyclonal antibodies to human interferon gamma in standard therapy reduced the overall duration of the disease on the average by 2 days as well as the duration of the main clinical symptoms, particularly hepatomegaly and knotty erythema. No exacerbations or recurrence of the disease were detected. No undesirable effects were registered upon administration of the preparation.

The efficacy and safety of the claimed preparation in the complex therapy of pseudotuberculosis in children have thus been shown.

Example 37.

The efficacy of ultra-low doses of antibodies to human interferon gamma in the conditions of influenza infection in wild type mice of both genders (n=120) was studied at the State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Russia. The infection process was modeled by the aerogenic introduction (through aerosol) of the influenza virus (strain A/Aichi/2/68 (H3N2) in the doses equal to 50-100 AID50 (aerogenic infective dose)) to mice lacking antibodies to the influenza A virus. Ultra-low doses (C12+C30+C50) of the polyclonal rabbit antibodies to human interferon gamma were administered intragastrically (0.2 ml/mouse/day). The reduction of the influenza virus titer in the lungs of infected mice compared to the control group was measured on days 2, 3, 4, and 5 after the infection.

The study showed that ultra-low doses of the antibodies to human interferon gamma reduced the titer of the influenza virus in the lungs of animals, as compared to the control group: by a factor of 2.7 (on day 2 or infection) in the case of prophylactic treatment and by a factor of 4.6 (on day 4 of infection) in the case of therapeutic treatment ($p<0.05$).

The prophylactic and therapeutic antiviral efficacy of the claimed preparation in the conditions of aerogenic influenza virus infection in mice have thus been shown.

Example 38.

The efficacy of ultra-low doses of antibodies to human interferon gamma in the conditions of herpes virus infection was studied at the State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Russia. The white wild type mice of both genders (n=60) were infected intraperitoneally with the herpes virus type II (HSV 2) in the dose equal to 5LD50. Ultra-low doses (C12+C30+C50) of the antibodies to human interferon gamma were administered intraabdominally (0.2 ml/mouse/day during 5 days). The effect was evaluated by the the concentration of the virus in the animal brain on days 2, 4, 6, 9, and 12 following the infection and by the survival of the mice on day 12 after the infection, as compared to the control group.

The comparison with the control group showed that ultra-low doses of the antibodies to human interferon gamma supressed the accummulation of the virus in the animal brain by a factor of 10 ($p < 0.05$), increased survival of the mice at all times following the infection and increased the mean life span of the animals by 3.3 days ($p < 0.05$).

The antiviral efficacy of the claimed preparation in the conditions herpes virus infection in mice has thus been shown.

Example 39.

The antiviral activity of ultra-low doses of antibodies to human interferon gamma in genital herpes models in comparison with acyclovir was studied at the N.F.Gamaleya Institute for Epidemiology & Microbiology, Moscow, Russia. 60 guinea pigs of the type «Smooth-Furred Agouti» (400-420 g) were infected with the genital herpes virus type II (VPG-2, EC strain). Ultra-low doses (C12+C30+C50) of the antibodies to human interferon gamma were administered intragastrally in a prophylactic (15 days) and therapeutic/prophylactic (20 days) regimens. The animals in the comparison group received acyclovir (100 mg/kg/day); the animals in the control group were injected with distilled water. The evaluation parameters included localized symptoms of genital herpes, general condition of the animals and the titer of the virus in vaginal smears.

The study showed that the therapeutic and especially therapeutic/prophylactic use of ultra-low doses of the antibodies to human interferon gamma significantly reduced the severety and duration of the general and localized symptoms of the herpes infection and significantly decreased the virus shedding by supressing its effect on the mucosa. In the case of therapeutic/prophylactic administration, the interferon antibodies were more effective than acyclovir.

The antiviral efficacy of the claimed preparation in the conditions of herpes virus infection in guinea pigs has thus been shown.

Example 40.

The efficacy of ultra-low doses of antibodies to human interferon gamma in the conditions of influenza infection in female mice of the line Balb/c (n=330) was studied at the State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Russia. The infection process was modeled by the intranasal introduction of the influenza virus (strain A/Aichi/2/68 (H3N2) in the dose equal to 1LD50 (sublethal infection) and 4LD50 (lethal infection)). Ultra-low doses

(C12+C30+C50) of the polyclonal rabbit antibodies to human interferon gamma were administered intragastrically (0.4 ml/mouse/day) during 5 days before the infection and 21 days after the infection. The comparison treatment (tamiflu, 10 mg/kg/day) was administered intragastrically (5mg/kg 2 times/day) during 5 days after the infection and then substituted by the distilled water on days 6-21 after the infection. The control group of animals received distilled water intragastrically. In the case of lethal infections, the survival of animals was evaluated; in the case of sublethal infections, the influenza virus titer in the lungs of the mice was evaluated on days 1, 3, 4, 6 after the infection.

The study showed that the administration of ultra-low doses of the antibodies to human interferon gamma in the cases of lethal infection increased survival of the animals more than by a factor of 2 and reduced the titer of the influenza virus in the lungs of animals by a factor of 4 (on day 3 of infection), as compared to the control group.

The prophylactic and therapeutic antiviral efficacy of the claimed preparation in the conditions of influenza virus infection in mice have thus been shown.

Example 41.

The efficacy of aqueous solution of ultra-low doses of antibodies to chicken interferon gamma (C12+C30+C200) in the prophylactic and therapeutic treatment of Leghorn laying hens (1000 g) infected by respiration with lethal doses (3 LD50) of the avian infulenza virus H5N1 was studied at the State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Russia. The preparation was administered in free access during 2 days before the infection and 7 days after the infection (the animals in the control group received distilled water in a similar regimen).

As a result of the infection with the lethal virus dose, the hens in the studied groups died before the development of any clinical symptoms of the disease. Ultra-low doses of antibodies to chicken interferon gamma showed antiviral activity with respect to the avian influenza virus. The free-access administration of the preparation to the hens that received a 3 LD50 infection dose increased the percentage of surviving hens by a factor of 2.2 compared to the control (11 hens out of 20 survived in the main group and 5 out of 20 in the control). 4 days after the infection the concentration of the influenza virus in the lungs of the hens was on the average 12% higher in the control group than in the main group that received the claimed preparation.

The above study demonstrates that the claimed preparation supresses the development of the infectious process in the lungs of birds infected by the lethal dose of the avian influenza virus and reduces lethal outcome in hens infected with the avian influenza virus.

Example 42.

The efficacy of aqueous solution of ultra-low doses of antibodies to chicken interferon gamma (C12+C30+C200) in the prophylactic and therapeutic treatment of Leghorn laying hens (1000 g) infected by respiration with lethal doses (3 LD50) of the avian infulenza virus H5N1 was studied at the State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Russia. The preparation was administered in free access during 2 days before the infection and 7 days after the infection (the animals in the control group received distilled water in a similar regimen).

The free-access administration of the preparation to hens infected with 3 ID50 doses increased the percentage of surved hens by a factor of 2.5 compared to the control (18 out of 20 hens

survived in the main group and 15 in the control group). Clinical symptoms of the disease were detected in both groups only in the hens that died after the infection with the 3 ID50 dose. In those cases, the following visual symptoms of the disease were registered: 1) apathy and inhibition; 2) photophobia; 3) distorted coordination; 4) convulsions; 5) meningeal symptoms at the moment of death. The number of the clinical symptoms in the hens that received the claimed preparation was lower by a factor of 1.8 than that in the control group (on per animal basis). On the fourth day of the infection, the concentration of the influenza virus in the lung tissue of the animals was on the average 15% higher in the control group than in the group that received the claimed preparation.

The above study demonstrates that the claimed preparation was effective in the therapeutic/prophylactic treatment of hens infected with a sublethal dose of the avian influenza virus which was expressed in its ability to increase the percentage of surviving infected birds and inhibit the reproduction of the virus in the animal lung tissues.

Example 43.

The effect of ultra-low doses of antibodies to human interferon gamma on the humoral immune response was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. CBA-line mice were one time immunized intraperitoneally with minimal doses ($5x10^6$/ml) of sheep erythrocytes (thymus-dependent corpuscular antigen) in the beginning of a 5-day treatment by the preparation containing ultra-low doses of antibodies to human interferon gamma (C12+C30+C50). The animals in the control group received distilled water. The experiments were conducted with healthy and immunosuppressed animals in parallel. In the beginning of the treatment with ultra-low doses of antibodies to human interferon gamma, animals received one-time intraperitoneal injections with 125 mg/kg doses of cyclophosphane to model immunosupression.

The results of the treatment with ultra-low doses of antibodies to human interferon gamma obtained on day 5 after immunization demonstrate an increase in the percentage of antibody producing cells in the spleen: by a factor of 1.5 in the healthy animals and by a factor of 1.7 in the case of cytostatic immunosupression induced by the injection of cyclophosphane in mice.

The claimed preparation has thus been demonstrated to promote a significant activation of the humoral response.

Example 44.

The effect of ultra-low doses of antibodies to human interferon gamma on the cellular immune response (intensity of the delayed hypersensitivity (DH) reaction) was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. CBA- and CBAxC57Bl/6-line mice were one time immunized with sheep erythrocytes (SE) in the end of a 10-day oral administration of the preparation containing ultra-low doses of antibodies to human interferon gamma (C12+C30+C50), doses 0.2 ml/mouse. A resolving dose of SE was injected in the rear paw pad on day 5 after the beginning of immunization. The animals in the control group were injected with distilled water. In a separate series of experiments, a part of the animals were intraperitoneally injected, upon setting the DH reaction, with a specific inhibitor of NO-synthase, NMMA (NG-monomethyl-L-arginine) on days 4 and 5 following the immunization. The intensity of the reaction was evaluated in each animal by the reaction index.

The results of the study demonstrated that upon treatment with ultra-low doses of antibodies to human interferon gamma the DH reaction index increased from 21.1±3.1 to 36.5±5.0 in response to the sensitization with sheep erythrocytes. The suppression of the nitric oxide (NO) production upon introduction of the NO-synthase inhibitor NMMA in vivo cancelled the above increase: the DH reaction index was lowered to 10.5±3.1 and 10.8±3.7, respectively.

The treatment with the claimed preparation has thus promoted a significant increase in the cellular immune response. The activation of the cellular immune response which disappeared upon the supression of NO synthesis served as an indirect evidence of the claimed preparation acting via interferon gamma.

Example 45.

The effect of ultra-low doses of antibodies to human interferon gamma on the phagocyte activity of neutrophils and macrophages in the peritoneal exudate of CBA-line female mice (n=48) was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. The ability of such cell to absorb one-day old culture of St. aureus was evaluated 24 h after the termination of a 10-day long treatment of the mice by ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) in the amount of 0.2 ml/mouse. The animals in the control group received distilled water. The evaluated parameters were the percentage of neutrophils or macrophages absorbed the microbes (the phagocyte index) and the mean number of staphyllococci absorbed by a single cell (the phagocyte number).

The oral treatment with ultra-low doses of antibodies to human interferon gamma increased the percentage of neutrophils capable of absorbing staphillococci from 21.3±0.8% in the control to 26.0±0.95% and increased the phagocyte activity of the peritoneal macrophages: the phagocyte index increased from 12.2±0.9% to 19.7±1.1%.

The oral treatment with the claimed preparation thus increased the phagocyte activity of neutrophyls and macrophages due to the increase in the number of the active phagocytes.

Example 46.

The effect of ultra-low doses of antibodies to human interferon gamma in vitro on the functional activity of natural killer lymphocytes (NK) was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. The suspension of mononuclear cells (MNC) used in the study was taken from the peripheral blood of healthy donors.

An aqueous solution of ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) was added to a complete growth media in the ratio of 50 µl per one ml of the media. The functional activity of NK was determined using the radiometric method in a cytotoxic reaction based on their ability to to lyse the cells of the myeloblastoid line K-562.

The addition of ultra-low doses of antibodies to human interferon gamma to the MNC culture increased the cytotoxicity index at the ratio of target cells to effector cells (1:25) from 63.6±2.7 to 71.7±1.9.

The claimed preparation has thus been demonstrated to increase in vitro the functional activity of NK which play an important role in the protection of the organism from intracellular parasites and tumor cells.

Example 47.

The effect of ultra-low doses of antibodies to human interferon gamma on the T-helper (CD4+)/T-supressor (CD8+) ratio in the spleen lymphocytes of CBA-line mice (n=30). The animals received ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) in the doses 0.2 ml/mouse during 1, 4, 7 and 10 days.

The results show that ultra-low doses of antibodies to human interferon gamma starting from day 4 of the treatment increase the CD4+/CD8+ ratio by a factor of 1.2 due to a decrease in CD8+ and a slight increase in CD4+.

The claimed preparation has thus been shown to increase the potential of preparedness of the immune system to the immune reaction.

Example 48.

The effect of extra ultra-low doses of antibodies to human interferon gamma on the proliferative activity of T- and B-lymphocytes was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. Mononuclear suspension from the periferal blood of healthy donors was used in the study. The proliferative activity of T- and B-lymphocytes was evaluated by blast-transformation reactions, both induced (by mixing 50 µl of mononuclears with 50 µl of mitogen and 50 µl of interferon antibodies) and spontaneous (by mixing 50 µl of mononuclears with 50 µl of interferon antibodies and 50 µl of the growth media). Phytohemagglutinin was used as the mitogen for T-lymphocytes, mitogen laconos – for B-lymphocytes. An aqueous solution of ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) was added to a complete growth media in the ratio of 50 µl per one ml of the media. 50 µl of the growth media was added to the control.

The results of the study showed that ultra-low doses of antibodies to human interferon gamma increased induced proliferation of T-lymphocytes by a factor of 1.7 and B-lymphocytes by a factor of 1.6 as compared to the control; however, they did not affect spontaneous proliferation of the lymphocytes.

The claimed preparation thus increases proliferative activity of T- and B-lymphocytes.

Example 49.

The effect of ultra-low doses of antibodies to human interferon gamma on the ability of spleenocytes to produce functionally active interferon gamma was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. CBA mice (n=24) were treated with ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) during 5 days. The level of production of human interferon gamma by spleenocytes was determined indirectly by the the ability of their supernatants to induce the synthesis of nitric oxide (NO) by the bone marrow cells. The amount of interferon gamma secreted by the spleen T-lymphocytes spontaneously and following mitogen activation was determined by the content of nitrites measured with the aid of the Griess reagent.

As a result of the treatment with the claimed preparation, the mice spleenocytes produced ex vivo 12 times more of functionally active interferon gamma.

It has thus been shown that the treatment of animals with the claimed preparation stimulates production of interferon gamma by the spleenocytes.

Example 50.

The effect of ultra-low doses of antibodies to human interferon gamma on the ability of spleenocytes to produce interferon gamma, interleukin-2 (IL-2), interleukin-4 (IL-4), and interleukin-10 (IL-10) was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. CBA/CaLac mice (n=204) used in the experiment received ultra-low doses of antibodies to human interferon gamma (C12+C30+C50) during 10 days. The animals in the control group were injected with distilled water. The spleenocytes were incubated for 24 h either without phytohemagglutinin (spontaneous experiment) or with the addition of phytohemagglutinin (PHG) (stimulated experiment). The content of interferon gamma, IL-2, IL-4, and IL-10 was quantified by solid-phase immunoenzyme assay.

The experiments showed that the treatment with ultra-low doses of antibodies to human interferon gamma increased spontaneous production of interferon gamma by the lymphocytes by more than a factor of 8 compared to its original level and by a factor of 6.5 compared to the control group.

The production of IL-2 increased from 42.1±2.9 to 61.1±7.7 pg/ml and from 38.7±2.8 to 56.5±5.7 pg/ml on days 3 and 7 of the experiment, respectively. The production of IL-4 increased from 5.4±0.2 to 16.4±4.1 pg/ml (198%) and from 5.2±0.2 to 7.4±0.8 pg/ml (41.7%) on days 7 and 10 of the experiment, respectively.

The treatment with ultra-low doses of antibodies to human interferon gamma did not affect spontaneous production of IL-10 by the spleen lymphocytes, but significantly increased its PHG-stimulated production on days 1-5 of the experiment, as compared to the control group (by 40.6-84.5%).

The oral treatment with the claimed preparation has thus been shown to affect not only the production of interferon gamma itself, but also production fo a number of cytokines functionally related to it and produced by T-helpers of type I (IL-2) and T-helpers of type II (IL-4, IL-10). This explains the ability of the interferon antibodies to stimulate cellular and humoral immune responses.

Example 51.

Dose-response relationships and the specificity of the effect of ultra-low doses of antibodies to human interferon gamma was studied at the Research Institute of Pharmacology Tomsk Scientific Center, Tomsk, Russia. Ultra-low doses of antibodies to erythropoietin (C12+C30+C50), tumor nerosis factor alpha (C12+C30+C50), human interferon gamma (C12+C30+C50) and ultra-low doses of human interferon gamma in molar doses (C3) were injected intragastrically into CBA/CaLac-line mice (n=342) (volume 0.2 ml) during 10 days. Spontaneous ex vivo production of interferon gamma by the spleenocytes of the animals was then determined by solid-phase immunoenzyme assay.

The study showed that unlike ultra-low doses of antibodies to erythropoietin and tumor necrosis factor, the oral administration of ultra-low doses of antibodies to human interferon gamma, both in the molar dose and in the ultra-low dose, increased spontaneous production of interferon gamma by the lymphocites by more than a factor of 3.

The data obtained prove the single direction of the effects and the specificity of the effect of antibodies to human interferon gamma when used in molecular and ultra-low doses.

RESEARCH REPORT

Questions and Answers About Homeopathy

On this page:

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Medical Dictionary

Related Topics

- Are you considering using CAM?
- Selecting a CAM practitioner

Treatment Information

- By treatment or therapy
- By disease or condition

Homeopathy ("home-ee-AH-pah-thy"), also known as homeopathic medicine, is a form of health care that developed in Germany and has been practiced in the United States since the early 19th century. Homeopathic practitioners are commonly called homeopaths. This fact sheet answers some frequently asked questions on homeopathy and reviews scientific research on its use and effectiveness.

Key Points

- In homeopathy, a key premise is that every person has energy called a vital force or self-healing response. When this energy is disrupted or imbalanced, health problems develop. Homeopathy aims to stimulate the body's own healing responses.
- Homeopathic treatment involves giving extremely small doses of substances that produce characteristic symptoms of illness in healthy people when given in larger doses. This approach is called "like cures like."
- Various explanations have been proposed as to how homeopathy might work. However, none of these explanations has been scientifically verified.
- Research studies on homeopathy have been contradictory in their findings. Some analyses have concluded that there is no strong evidence supporting homeopathy as effective for any clinical condition. However, others have found positive effects from homeopathy. The positive effects are not readily explained in scientific terms.
- It is important to inform all of your health care providers about any therapy that you are currently using or considering, including homeopathic treatment. This is to help ensure a safe and coordinated course of care.

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1. What is homeopathy?

The term homeopathy comes from the Greek words *homeo*, meaning similar, and *pathos*, meaning suffering or disease. Homeopathy is an alternative medical system. Alternative medical systems are built upon complete systems of theory and practice, and often have evolved apart from and earlier than the conventional medical approach used in the United States.[a] Homeopathy takes a different approach from conventional medicine in diagnosing, classifying, and treating medical problems.

Key concepts of homeopathy include:

- Homeopathy seeks to stimulate the body's defense mechanisms and processes so as to prevent or treat illness.
- Treatment involves giving very small doses of substances called remedies that, according to homeopathy, would produce the same or similar symptoms of illness in healthy people if they were given in larger doses.
- Treatment in homeopathy is individualized (tailored to each person). Homeopathic practitioners select remedies according to a total picture of the patient, including not only symptoms but lifestyle, emotional and mental states, and other factors.

a. Conventional medicine, as defined by NCCAM, is medicine as practiced by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and by their allied health professionals, such as physical therapists, psychologists, and registered nurses. Some conventional medical practitioners are also practitioners of complementary and alternative medicine. To find out more about these terms, see the NCCAM fact sheet "What Is Complementary and Alternative Medicine?"

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2. What is the history of the discovery and use of homeopathy?[b]

In the late 1700s, Samuel Hahnemann, a physician, chemist, and linguist in Germany, proposed a new approach to treating illness. This was at a time when the most common medical treatments were harsh, such as bloodletting,[c] purging, blistering, and the use of sulfur and mercury. At the time, there were few effective medications for treating patients, and knowledge about their effects was limited.

Hahnemann was interested in developing a less-threatening approach to medicine. The first major step reportedly was when he was translating an herbal text and read about a treatment (cinchona bark) used to cure malaria. He took some cinchona bark and observed that, as a healthy person, he developed symptoms that were very similar to malaria symptoms. This led Hahnemann to consider that a substance may create symptoms that it can also relieve. This concept is called the "similia principle" or "like cures like." The similia principle had a prior history in medicine, from Hippocrates in Ancient Greece--who noted, for example, that recurrent vomiting could be treated with an emetic (such as ipecacuanha) that would be expected to make it worse--to folk medicine.[14,15] Another way to view "like cures like" is that symptoms are part of the body's attempt to heal itself--for example, a fever can develop as a result of an immune response to an infection, and a cough may help to eliminate mucus--and medication may be given to support this self-healing response.

Hahnemann tested single, pure substances on himself and, in more dilute forms, on healthy volunteers. He kept meticulous records of his experiments and participants' responses, and he combined these observations with information from clinical practice, the known uses of herbs and other medicinal substances, and toxicology,[d] eventually treating the sick and developing homeopathic clinical practice.

Hahnemann added two additional elements to homeopathy:

- A concept that became "potentization," which holds that systematically diluting a substance, with vigorous shaking at each step of dilution, makes the remedy more, not less, effective by extracting the vital essence of the substance. If dilution continues to a point where the substance's molecules are gone, homeopathy holds that the "memory" of them--that is, the effects they exerted on the surrounding water molecules--may still be therapeutic.
- A concept that treatment should be selected based upon a total picture of an individual and his symptoms, not solely upon symptoms of a disease. Homeopaths evaluate not only a person's physical symptoms but her emotions, mental states, lifestyle, nutrition, and other aspects. In homeopathy, different people with the same symptoms may receive different homeopathic remedies.

Hans Burch Gram, a Boston-born doctor, studied homeopathy in Europe and introduced it into the United States in 1825. European immigrants trained in homeopathy also made the treatment increasingly available in America. In 1835, the first homeopathic medical college was established in Allentown, Pennsylvania. By the turn of the 20th century, 8 percent of all American medical practitioners were homeopaths, and there were 20 homeopathic medical colleges and more than 100 homeopathic hospitals in the United States.

In the late 19th and early 20th centuries, numerous medical advances were made, such as the recognition of the mechanisms of disease; Pasteur's germ theory; the development of antiseptic techniques; and the discovery of ether anesthesia. In addition, a report (the so-called "Flexner Report") was released that triggered major changes in American medical education. Homeopathy was among the disciplines negatively affected by these developments. Most homeopathic medical schools closed down, and by the 1930s others had converted to conventional medical schools.

In the 1960s, homeopathy's popularity began to revive in the United States. According to a 1999 survey of Americans and their health, over 6 million Americans had used homeopathy in the preceding 12 months.[16] The World Health Organization noted in 1994 that homeopathy had been integrated into the national health care systems of numerous countries, including Germany, the United Kingdom, India, Pakistan, Sri Lanka, and Mexico.[7] Several schools of practice exist within homeopathy.[17]

Persons using homeopathy do so to address a range of health concerns, from wellness and prevention to treatment of injuries, diseases, and conditions. Studies have found that many people who seek homeopathic care seek it for help with a chronic medical condition.[18,19,20] Many users of homeopathy treat themselves with homeopathic products and do not consult a professional.[13]

b. Items 1-13 in the references served as general sources for this historical discussion.

c. Bloodletting was a healing practice used for many centuries. In bloodletting, incisions were made in the body to drain a quantity of blood, in the belief that this would help drain out the "bad blood" or sickness.

d. Toxicology is the science of the effects of chemicals on human health.

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3. What kind of training do homeopathic practitioners receive?

In European countries, training in homeopathy is usually pursued either as a primary professional degree completed over 3 to 6 years or as postgraduate training for doctors.[14]

In the United States, training in homeopathy is offered through diploma programs, certificate programs, short courses, and correspondence courses. Also, homeopathic training is part of medical education in naturopathy.[e] Most homeopathy in the United States is practiced along with another health care practice for which the practitioner is licensed, such as conventional medicine, naturopathy, chiropractic, dentistry, acupuncture, or veterinary medicine (homeopathy is used to treat animals).

Laws about what is required to practice homeopathy vary among states. Three states (Connecticut, Arizona, and Nevada) license medical doctors specifically for homeopathy.

e. Naturopathy, also known as naturopathic medicine, is an alternative medical system that emphasizes natural healing approaches (such as herbs, nutrition, and movement or manipulation of the body). Some elements of naturopathy are similar to homeopathy, such as an intent to support the body's own self-healing response.

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4. What do homeopathic practitioners do in treating patients?

Typically, in homeopathy, patients have a lengthy first visit, during which the provider takes an in-depth assessment of the patient. This is used to guide the selection of one or more homeopathic remedies. During followup visits, patients report how they are responding to the remedy or remedies, which helps the practitioner make decisions about further treatment.

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5. What are homeopathic remedies?

Most homeopathic remedies are derived from natural substances that come from plants, minerals, or animals. A remedy is prepared by diluting the substance in a series of steps (as discussed in Question 2). Homeopathy asserts that this process can maintain a substance's healing properties regardless of how many times it has been diluted. Many homeopathic remedies are so highly diluted that not one molecule of the original natural substance remains.[12,21] Remedies are sold in liquid, pellet, and tablet forms.

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6. How does the U.S. Food and Drug Administration (FDA) regulate homeopathic remedies?

Because of their long use in the United States, the U.S. Congress passed a law in 1938 declaring that homeopathic remedies are to be regulated by the FDA in the same manner as nonprescription, over-the-counter (OTC) drugs, which means that they can be purchased without a physician's prescription. Today, although conventional prescription drugs and new OTC drugs must undergo thorough testing and review by the FDA for safety and effectiveness before they can be sold, this requirement does not apply to homeopathic remedies.

Remedies are required to meet certain legal standards for strength, quality, purity, and packaging. In 1988, the FDA required that all homeopathic remedies list the indications for their use (i.e., the medical problems to be treated) on the label.[22,23] The FDA also requires the label to list ingredients, dilutions, and instructions for safe use.

The guidelines for homeopathic remedies are found in an official guide, the *Homeopathic Pharmacopoeia of the United States*, which is authored by a nongovernmental, nonprofit organization of industry representatives and homeopathic experts.[24] The *Pharmacopoeia* also includes provisions for testing new remedies and verifying their clinical effectiveness. Remedies on the market before 1962 have been accepted into the *Homeopathic Pharmacopoeia of the United States* based on historical use, rather than scientific evidence from clinical trials.

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7. Have any side effects or complications been reported from the use of homeopathy?

The FDA has learned of a few reports of illness associated with the use of homeopathic remedies. However, the FDA reviewed these reports and decided that the remedies were not likely to be the cause, because of the high dilutions.[3]

Here is some general information that has been reported about risks and side effects in homeopathy:

- Homeopathic medicines in high dilutions, taken under the supervision of trained professionals, are considered safe and unlikely to cause severe adverse reactions.[25]
- Some patients report feeling worse for a brief period of time after starting homeopathic remedies. Homeopaths interpret this as the body temporarily stimulating symptoms while it makes an effort to restore health.
- Liquid homeopathic remedies can contain alcohol and are permitted to have higher levels of alcohol than conventional drugs for adults. This may be of concern to some consumers. However, no adverse effects from the alcohol levels have been reported either to the FDA or in the scientific literature.[3]
- Homeopathic remedies are not known to interfere with conventional drugs; however, if you are considering using homeopathic remedies, you should discuss this with your health care provider. If you have more than one provider, discuss it with each one.

As with all medicinal products, a person taking a homeopathic remedy is best advised to:

- Contact his health care provider if his symptoms continue unimproved for more than 5 days.
- Keep the remedy out of the reach of children.
- Consult a health care provider before using the product if the user is a woman who is pregnant or nursing a baby.

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8. What has scientific research found out about whether homeopathy works?

This section summarizes results from (1) individual clinical trials (research studies in people) and (2) broad analyses of groups of clinical trials.

The results of individual, controlled clinical trials of homeopathy have been contradictory. In some trials, homeopathy appeared to be no more helpful than a placebo; in other studies, some benefits were seen that the researchers believed were greater than one would expect from a placebo.[f] Appendix I details findings from clinical trials.

Systematic reviews and meta-analyses take a broader look at collections of a set of results from clinical trials.[g] Recent examples of these types of analyses are detailed in Appendix II. In sum, systematic reviews have not found homeopathy to be a definitively proven treatment for any medical condition. Two groups of authors listed in Appendix II found some positive evidence in the groups of studies they examined, and they did not find this evidence to be explainable completely as placebo effects (a third group found 1 out of 16 trials to have some added effect relative to placebo). Each author or group of authors criticized the quality of evidence in the studies. Examples of problems they noted include weaknesses in design and/or reporting, choice of measuring techniques, small numbers of participants, and difficulties in replicating results. A common theme in the reviews of homeopathy trials is that because of these problems and others, it is difficult or impossible to draw firm conclusions about whether homeopathy is effective for any single clinical condition.

f. A placebo is designed to resemble as much as possible the treatment being studied in a clinical trial, except that the placebo is inactive. An example of a placebo is a pill containing sugar instead of the drug or other substance being studied. By giving one group of participants a placebo and the other group the active treatment, the researchers can compare how the two groups respond and get a truer picture of the active treatment's effects. In recent years, the definition of placebo has been expanded to include other things that could have an effect on the results of health care, such as how a patient and a health care provider interact, how a patient feels about receiving the care, and what he or she expects to happen from the care.

g. In a systematic review, data from a set of studies on a particular question or topic are collected, analyzed, and critically reviewed. A meta-analysis uses statistical techniques to analyze results from individual studies.

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9. Are there scientific controversies associated with homeopathy?

Yes. Homeopathy is an area of complementary and alternative medicine (CAM) that has seen high levels of controversy and debate, largely because a number of its key concepts do not follow the laws of science (particularly chemistry and physics).

- It is debated how something that causes illness might also cure it.
- It has been questioned whether a remedy with a very tiny amount (perhaps not even one molecule) of active ingredient could have a biological effect, beneficial or otherwise.

  There have been some research studies published on the use of ultra-high dilutions (UHDs) of substances, diluted to levels compatible with those in homeopathy and shaken hard at each step of dilution.[h] The results are claimed to involve phenomena at the molecular level and beyond, such as the structure of water, and waves and fields. Both laboratory research and clinical trials have been published. There have been mixed results in attempts to replicate them. Reviews have not found UHD results to be definitive or compelling.[i]

  There have been some studies that found effects of UHDs on isolated organs, plants, and

animals.[15] There have been controversy and debate about these findings as well.

- Effects in homeopathy might be due to the placebo or other non-specific effect.
- There are key questions about homeopathy that are yet to be subjected to studies that are well-designed--such as whether it actually works for some of the diseases or medical conditions for which it is used, and if so, how it might work.
- There is a point of view that homeopathy does work, but that modern scientific methods have not yet explained why. The failure of science to provide full explanations for all treatments is not unique to homeopathy.
- Some people feel that if homeopathy appears to be helpful and safe, then scientifically valid explanations or proofs of this alternative system of medicine are not necessary.

h. For some examples, see references 26-29.

i. For examples of debates on UHDs and reviewers' papers, see especially references 13, 15, and 30-33.

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10. Is NCCAM funding research on homeopathy?

Yes, NCCAM supports a number of studies in this area. For example:

- Homeopathy for physical, mental, and emotional symptoms of fibromyalgia (a chronic disorder involving widespread musculoskeletal pain, multiple tender points on the body, and fatigue).
- Homeopathy for brain deterioration and damage in animal models for stroke and dementia.
- The homeopathic remedy cadmium, to find out whether it can prevent damage to the cells of the prostate when those cells are exposed to toxins.

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For More Information

- **NCCAM Clearinghouse**

  Toll-free in the U.S.: 1-888-644-6226
  International: 301-519-3153
  TTY (for deaf and hard-of-hearing callers): 1-866-464-3615

  E-mail: info@nccam.nih.gov
  NCCAM Web site: nccam.nih.gov
  Address: NCCAM Clearinghouse, P.O. Box 7923, Gaithersburg, MD 20898-7923

  Fax: 1-866-464-3616

  The NCCAM Clearinghouse provides information on CAM and on NCCAM. Services include fact sheets, other publications, and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

- **CAM on PubMed**

  Web site: www.nlm.nih.gov/nccam/camonpubmed.html

  CAM on PubMed, a database on the Internet developed jointly by NCCAM and the National Library of Medicine, offers citations to (and in most cases, brief summaries of) articles on CAM in scientifically based, peer-reviewed journals . CAM on PubMed also links to many publisher Web sites, which may offer the full text of articles.

- **U.S. Food and Drug Administration (FDA)**

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German Homoeopathic Pharmacopoeia, 5th Supplement to 1978 edition

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General Regulations for the Manufacture of Homoeopathic Drugs

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Zimpel's spagyric mother tinctures	Methods 25-26

MANUFACTURE

Method 1: Mother tinctures and liquid dilutions
Mother tinctures by Method 1 are mixtures of equal parts of expressed juice and ethanol 86 per cent.

Express the finely cut plants or parts of plants, and immediately mix the expressed fluid with an equal part by weight of ethanol 86 per cent. Leave to stand in a closed container for not less than 5 days at a temperature not exceeding 20 °C; filter.

Adjustment to any parameter given in the Monograph
Determine the dry residue or solid content of the above filtrate. Calculate the amount of ethanol 43 per cent (E_1) required, using Formula (1):

$$E_1 = \frac{W\,(N_x - N_0)}{100}\ [kg] \qquad (1)$$

W = weight of filtrate in kg
N_0 = dry residue or solid content in per cent as required by Monograph
N_x = dry residue or solid content of filtrate in per cent.

Combine the filtrate with the required amount of ethanol 43 per cent. Leave to stand at a temperature not exceeding 20 °C for not less than 5 days; filter if necessary.

Potentization
The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 43 per cent,

the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 43 per cent.
Subsequent dilutions are produced in the same way.

The 1st centesimal dilution (1c) is made with
2 parts of the mother tincture and
98 parts of ethanol 43 per cent,

the 2nd centesimal dilution (2c) with
1 part of the 1 st centesimal dilution and
99 parts of ethanol 43 per cent.
Subsequent dilutions are produced in the same way.

Method 2a: Mother tinctures and liquid dilutions
Mother tinctures manufactured by Method 2a are produced by macerating the

material as described below (ethanol content approx. 43 per cent).

The plants or parts of plants are finely minced. A sample is used to determine loss on drying. To the minced plant material add immediately not less than half the amount by weight of ethanol 86 per cent and store in well sealed containers at a temperature not exceeding 20 °C.

Calculate the amount of ethanol 86 per cent required (E_2), for the plant material, using Formula (2), deduct the amount of ethanol that has already been used, and add the final amount to the mixture.

$$E_2 = \frac{M \cdot D}{100} \text{ [kg]} \qquad (2)$$

M = weight of plant material in kg
D = loss on drying in sample, in per cent.

Leave the mixture to stand for not less than 10 days at a temperature not exceeding 20 °C, shaking repeatedly. Express and filter.

Adjust to any parameters given in the Monograph, as for Method 1.

Potentize as shown under Method 1.

Method 2b: Mother tinctures and liquid dilutions

Mother tinctures made in accordance with Method 2b are manufactured as per Method 2a, using ethanol 62 per cent (ethanol content approx. 30 per cent).

Use ethanol 30 per cent to adjust to any concentration required in the Monograph.

Potentization

The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 30 per cent,

the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 15 per cent.

Subsequent dilutions are produced in the same way.

Method 3a: Mother tinctures and liquid dilutions

Mother tinctures for Method 3a are produced according to Method 2a (ethanol content approx. 60 per cent), with the following difference: The required amount of ethanol 86 per cent (E_3), is calculated according to Formula (3).

$$E_3 = \frac{2 \cdot M \cdot D}{100} \text{ [kg]} \qquad (3)$$

M = weight of plant material in kg
D = loss on drying in sample, in per cent.
Use ethanol 62 per cent to adjust to any concentration required as per Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 62 per cent,

the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 62 per cent.
Subsequent dilutions are produced in the same way. For dilutions from the 4th decimal onwards use ethanol 43 per cent.

The 1st centesimal dilution (1c) is made with
3 parts of the mother tincture and
97 parts of ethanol 62 per cent,

the 2nd centesimal dilution (2c) with
1 part of the 1st centesimal dilution and
99 parts of ethanol 43 per cent.
Subsequent dilutions are produced in the same way.

Method 3b: Mother tinctures and liquid dilutions
Mother tinctures for Method 3b are produced according to Method 3a, using ethanol 73 per cent (ethanol content approx. 43 per cent).
Use ethanol 43 per cent to adjust to any concentration required in the Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 43 per cent,

the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 30 per cent,
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

Method 3c: Mother tinctures and liquid dilutions
Mother tinctures for Method 3c are produced according to Method 3a using, ethanol 43 per cent (ethanol content approx. 30 per cent).
Use ethanol 30 per cent to adjust to any concentration required in the Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 30 per cent,

the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

Method 4a: Mother tinctures and liquid dilutions
Method 4a is for mother tinctures manufactured according to the maceration or percolation methods described in the TINKTUREN (tinctures) Monograph in the German Pharmacopoeia using 1 part of the drug to 10 parts of ethanol in suitable concentration (unless otherwise stated in the Monograph). If adjustment to a given value is necessary, the required amount of ethanol in the concentration prescribed or used for manufacture is calculated according to Formula (1). The calculated amount of ethanol is combined with the filtrate. The mixture is left to stand for not less than five days at a temperature not exceeding 20 °C, after which it is filtered if required.

Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).

The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol of the same concentration.

the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol of the same concentration.
Ethanol 43 per cent is used for subsequent dilutions from the 4th decimal upwards unless a different concentration is prescribed; the method is the same as for the 3rd decimal dilution.

The 1st centesimal dilution (1c) is made with
10 parts of the mother tincture and
90 parts of ethanol of the same concentration.

the 2nd centesimal dilution (2c) with
1 part of the 1st centesimal dilution and
99 parts of ethanol 43 per cent, unless another concentration is prescribed.
Subsequent dilutions are produced in the same way.

Method 4b: Mother tinctures and liquid dilutions
Method 4b is for mother tinctures manufactured according to the maceration or

percolation methods described in the TINKTUREN (tinctures) Monograph in the German Pharmacopoeia using 1 part of animals, parts of animals or animal secretions and 10 parts of ethanol in suitable concentration. If adjustment to a given value is necessary, the required amount of ethanol in the concentration prescribed or used for manufacture is calculated according to Formula (1). The calculated amount of ethanol is combined with the filtrate. The mixture is left to stand for not less than five days at a temperature not exceeding 20 °C, after which it is filtered if required.

Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).

The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol of the same concentration.

the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol of the same concentration.
Ethanol 43 per cent is used for subsequent dilutions from the 4th decimal upwards; the method is the same as for the 3rd decimal dilution.

The 1st centesimal dilution (1c) is made with
10 parts of the mother tincture and
90 parts of ethanol of the same concentration.

the 2nd centesimal dilution (2c) with
1 part of the 1st centesimal dilution and
99 parts of ethanol 43 per cent.
Subsequent dilutions are produced in the same way.

Method 5a: Solutions
Liquid preparations made by Method 5a are solutions produced from basic drug materials and a liquid vehicle. Unless otherwise prescribed in the Monograph, 1 part of the basic drug material is dissolved in 9 parts (= 1x) or 99 parts (= 1c or 2x) of the liquid vehicle and succussed. Absolute ethanol, purified water, glycerol 85 per cent and the ethanol/water mixtures listed in the GHP are used as vehicles.

If ethanol 15 per cent is the prescribed vehicle for the liquid preparation, the solution may also be produced by the following method: 1 part of the basic drug material is dissolved in 7.58 parts of water, to produce the 1x; add 1.42 parts of ethanol to the solution. To produce the 1c or 2x, 1 part of the basic drug material is dissolved in 83.4 parts of water, adding 15.6 parts of ethanol to the solution.

Potentization
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol 43 per cent,

unless another vehicle is prescribed. Subsequent dilutions are produced in the same way.

The 2nd centesimal dilution (2c) is made with
1 part of the 1st centesimal dilution (1c) and
99 parts of ethanol 43 per cent,
unless another liquid vehicle is prescribed. Subsequent dilutions are produced in the same way.

Method 5b: Aqueous solutions
Liquid preparations made by Method 5b are solutions produced from basic drug materials and WATER FOR INJECTIONS. Unless otherwise stated in the Monograph, 1 part of the basic drug material is dissolved in 9 parts (= 1x) or 99 parts (= 1c or 2x) of WATER FOR INJECTIONS and succussed.

Potentization
The 2nd decimal dilution (2x) is made with
1 part of the solution (1x) and
9 parts of WATER FOR INJECTIONS.
Subsequent dilutions are produced in the same way.

Aqueous solutions produced by Method 5b are normally processed immediately; their use is limited to the manufacture of preparations by Methods 11, 13, 14, 15, 39a and 39c.

Solutions made according to Method 5b and their liquid dilutions must comply with the 'Sterility Test' given in the German Pharmacopoeia if stored.

LABELLING
Preparations made according to Method 5b carry the designation 'aquos.' after the indication of the potency; the same applies to presentations made from them.

Method 6: Triturations
Preparations made according to Method 6 are triturations of solid basic drug materials with lactose as the vehicle unless otherwise prescribed. Triturations up to and including the 4th dilution are triturated by hand or machine in a ratio of 1 to 10 (decimal dilution) or 1 to 100 (centesimal dilution). Unless otherwise stated, the basic drug materials are reduced to the particle size given in the Monograph (mesh aperture). Quantities of more than 1,000 g are triturated by mechanical means.

The duration and intensity of trituration should be such that the resulting particle size of the basic drug material in the 1st decimal or centesimal dilution is below 10 μm at 80 per cent level; no drug particle should be more than 50 μm.

Triturations up to and including the 4th decimal or centesimal are produced at the same duration and intensity of trituration.

Trituration by hand
Divide the vehicle into three parts and triturate the first part for a short period in a porcelain mortar. Add the basic drug material and triturate for 6 minutes, scrape

down for 4 minutes with a porcelain spatula, triturate for a further 6 minutes, scrape down again for 4 minutes, add the second part of the vehicle and continue as above. Finally add the third part and proceed as before. The minimum time required for the whole process will thus be 1 hour. The same method is followed for subsequent dilutions.

For triturations above the 4x or 4c dilute 1 part of the dilution with 9 parts of lactose or 99 parts of lactose as follows: in a mortar, combine one third of the required amount of lactose with the whole of the previous dilution and mix until homogeneous. Add the second third of the lactose, mix until homogeneous, and repeat for the last third.

Trituration by machine

Up to and including the 4th dilution, triturations are made in a machine fitted with a scraping device that ensures even trituration.

Other machines may be used, providing the particle sizes produced meet requirements.

To produce a trituration by machine, triturate one third of the vehicle, add the basic drug material and triturate; finally add the remaining vehicle in two equal portions and triturate. The time required to produce one trituration by machine is not less than 1 hour.

Dilutions above the 4x or 4c are made by diluting 1 part of the dilution with 9 parts of lactose or 99 parts of lactose and combining one third of the required amount of lactose in a suitable mixer with the whole of the previous dilution and mixing until homogeneous. Add the second third of the lactose, mix until homogeneous, and proceed in the same way with the last third of the lactose.

The choice of a suitable mixer and the mixing time required to achieve homogeneity are established in a single trial run for each type of apparatus and recorded. Additional requirements relating to the machine in question are determined, recorded and written down in the operating instructions for the production process.

Method 7: Triturations

Preparations made by Method 7 are solid preparations of mother tinctures and solutions and their dilutions with lactose as the vehicle.

The total amount of lactose required is transferred to a suitable apparatus, and the prescribed amount of the liquid preparation in the previous dilution stage is gradually mixed in. The moist homogeneous mix is dried with care, ground if necessary and sieved before mixing again thoroughly.

The amount of lactose used should be such that the preparation will have the prescribed total weight when the manufacturing process is complete.

Quantities of more than 1,000 g are made by mechanical trituration; the type of mixer, mixing period, drying time and length of the final mixing stage are determined in a single trial run, recorded and written down in the operating instructions for the production process.

Potentization

Mother tinctures, solutions and liquid dilutions are potentized in the relative

quantities laid down for their production. Lactose serves as the vehicle; the amount of lactose added must be such that the total weight is 10 parts for decimal and 100 parts for centesimal potencies.

Method 8a: Liquid preparations made from triturations
Preparations made by Method 8a are liquid preparations produced from triturations made by Method 6.

To produce a 6x liquid dilution, 1 part of the 4x trituration is dissolved in 9 parts of water and succussed. 1 part of this dilution is combined with 9 parts of ethanol 30 per cent to produce the 6x liquid dilution by succussion. In the same way, the 7x liquid dilution is made from the 5x trituration, and the 8x liquid dilution from the 6x trituration. From the 9x upwards, liquid decimal dilutions are made from the previous decimal dilution with ethanol 43 per cent in a ratio of 1 to 10.

To produce a 6c liquid dilution, 1 part of the 4c trituration is dissolved in 99 parts of water and succussed. 1 part of this dilution is combined with 99 parts of ethanol 30 per cent to produce the 6c liquid dilution by succussion. In the same way, the 7c liquid dilution is made from the 5c trituration, and the 8c liquid dilution from the 6c trituration. From the 9c upwards, liquid centesimal dilutions are made from the previous centesimal dilution with ethanol 43 per cent in a ratio of 1 to 100.

The 6x, 7x, 6c and 7c liquid dilutions produced by the above method must not be used to produce further liquid dilutions.

Method 8b: Aqueous preparations made from triturations
Preparations made by Method 8b are aqueous preparations produced from triturations made by Method 6.

To produce a 6x liquid dilution, 1 part of the 4x trituration is dissolved in 9 parts of WATER FOR INJECTIONS and succussed. 1 part of this dilution is combined with 9 parts of WATER FOR INJECTIONS to produce the 6x liquid dilution by succussion. In the same way, the 7x liquid dilution is made from the 5x trituration, and the 8x liquid dilution from the 6x trituration. From the 9x upwards, liquid decimal dilutions are made from the previous decimal dilution with WATER FOR INJECTIONS in a ratio of 1 to 10.

6x and 7x liquid dilutions made by the above method must not be used to produce further liquid dilutions.

Aqueous preparations made by Method 8b are normally processed immediately; their use is limited to the manufacture of presentations by Methods 11, 13, 14, 15, 39a and 39c, mixtures by Method 16, and potentized mixtures by Method 40b.

Aqueous preparations made by Method 8b must comply with the 'Sterility Test' of the German Pharmacopoeia if stored.

LABELLING
Preparations made by Method 8b carry the designation 'aquos.' after the indication of the potency; the same applies to presentations made from them.

Method 9: Tablets
Tablets made by Method 9 are produced from preparations made by Method 6 or

Method 7.

Except for 'Uniformity of content' they must comply with the **Tablets** monograph for uncoated tablets in the German Pharmacopoeia.

Permitted excipients are starch—in concentrations of up to 10 per cent—and calcium behenate or magnesium stearate—in concentrations of up to 2 per cent. A saturated lactose solution or starch paste or ethanol in suitable concentration is used if granulation is required.

Tablets prepared solely from preparations produced by Method 6 or 7 are single doses containing 100 or 250 mg of the particular preparation. The weight of excipients is additional to this.

LABELLING

Tablets are labelled with the dilution stage in accord with preparation by Method 6 or 7.

Method 10: Granules (Globuli)

Preparations made by Method 10 are granules (globuli). They are produced by transferring a dilution to sucrose granules (size 3: 110-130 granules weigh 1 g) by moistening 100 parts of sucrose granules evenly with 1 part of dilution. The ethanol content of the dilution should be not less than 60 per cent. If this is not the case, it will be necessary to go against Methods 1 to 4b and produce the final potentization of the decimal or centesimal dilution which is to be used with ethanol 62 per cent.

Following impregnation in a closed vessel, the granules (globuli) are air-dried. They are labelled with the dilution stage of the dilution used to impregnate them.

The following granule sizes may be used in special cases:

Size 1	470-530	granules weigh 1 g
Size 2	220-280	granules weigh 1 g
Size 3	110-130	granules weigh 1 g
Size 4	70- 90	granules weigh 1 g
Size 5	40- 50	granules weigh 1 g
Size 6	22- 28	granules weigh 1 g
Size 7	10	granules weigh approx. 1 g
Size 8	5	granules weigh approx. 1 g
Size 9	3	granules weigh approx. 1 g
Size 10	2	granules weigh approx. 1 g

Method 11: Parenteral preparations

Preparations made by Method 11 are sterile, injectable dilutions of one or more homoeopathic preparations. They are designed for injection and must comply with the **Parenteralia** monograph in the German Pharmacopoeia. The only additives permitted are agents used to make the preparations isotonic and adjust the pH; preservatives may be used in specific cases. Sodium chloride is normally used to make preparations isotonic; other agents used for that purpose must be declared.

Parenteral preparations for human use are supplied in single-dose glass ampoules. Multi-dose glass containers may be used for veterinary preparations.

'Uniformity of content' tests (V.5.2.2) are not required.

With parenteral preparations produced from preparations containing ethanol, care is taken to keep the final ethanol content as low as possible.

This may be achieved by mixing and/or potentizing with water for injections or the solution of isotonizing agent. For potentization, an ethanol-free vehicle is used for the last two decimal dilution stages and the last centesimal dilution stage respectively.

LABELLING

Different potencies combined for further potentization must be stated. Added vehicles must be stated.

Method 12a: Liquid external applications

Preparations made by Method 12a are tinctures for external use produced as follows:

using mother tinctures made by Method 1 or 2a or 19a, combine
2 parts of the mother tincture with
3 parts of ethanol 43 per cent,

using mother tinctures made by Method 2b or 19b, combine
2 parts of the mother tincture with
3 parts of ethanol 30 per cent,

using mother tinctures made by Method 3a or 19c, combine
3 parts of the mother tincture with
2 parts of ethanol 62 per cent,

using mother tinctures made by Method 3b or 19d, combine
3 parts of the mother tincture with
2 parts of ethanol 43 per cent,

using mother tinctures made by Method 3c or 19e, combine
3 parts of the mother tincture with
2 parts of ethanol 30 per cent,

using mother tinctures made by Method 4a or 4b or 19f, combine
1 part of the mother tincture with
1 part of ethanol in the concentration used to make the mother tincture;

by extracting dried plants or parts of plants with ethanol in a ratio of 1 :5 (as per Method 4a or 19f).

Tinctures for external use may contain up to 10 per cent of glycerin as an additive.

NOTE

Tinctures for external use are not for internal use and are labelled to indicate this.

Method 12b: Liquid external applications
Preparations made by Method 12b are tinctures for external use produced by Method 2a with ethanol 73 per cent.

The Method differs from Method 2a in that the amount of ethanol 73 per cent required (E) is calculated using the following formula:

$$E = \frac{4 \cdot Mm \cdot D}{100} \quad [kg]$$

M = weight of plant material in kg
D = loss on drying in sample, in per cent.

LABELLING
Preparations made by Method 12b are labelled 'ad usum externum'.

Method 12c: Liquid external applications
Preparations made by Method 12c are tinctures for external use produced by maceration according to the following method:

Finely mince the plants or parts of plants, unless flowers only are used. Use a sample to determine loss on drying. To 1 part of the plant material add immediately 2.88 parts of water and 1.12 parts of ethanol and store at a temperature not exceeding 20 °C. The additional amount of water (W) required is calculated according to the formula:

$$W = \frac{M \cdot (100 - D)}{100} \quad [kg]$$

M = weight of plant material in kg
D = loss on drying in sample, in per cent,
and added to the mixture. Leave to stand for not less than 5 days at a temperature not exceeding 20 °C; stir the mixture every morning and evening during those 5 days. Express and filter.

LABELLING
Preparations made by Method 12c are labelled 'LE 20%'.

STORAGE
Protected from light.

Method 12d: Liquid external applications
Preparations made by Method 12d are oils for external use produced with 1 part of the dried plants or parts of plants and 10 parts of vegetable oil, using the method given below. Groundnut oil, olive oil or sesame oil are normally used; other oils

must be declared.

Moisten 1 part of the minced drug with 0.25 parts of ethanol. Cover and leave to stand for approx. 12 hours before combining with 10 parts of vegetable oil. Heat the mixture to 60 - 70 °C and maintain it at that temperature for approx. 4 hours. Express and filter.

LABELLING
Preparations made by Method 12d are labelled 'H 10%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12e: Liquid external applications
Preparations made by Method 12e are oils for external use produced with 1 part of the dried plants or parts of plants and 20 parts of vegetable oil, using the method given below. Groundnut oil, olive oil or sesame oil are normally used; other oils must be declared.

Moisten 1 part of the minced drug with 0.25 parts of ethanol. Cover and leave to stand for approx. 12 hours before combining with 20 parts of vegetable oil. Heat the mixture to 60 - 70 °C and maintain it at that temperature for approx. 4 hours. Express and filter.

LABELLING
Preparations made by Method 12e are labelled 'H 5%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12f: Liquid external applications
Preparations made by Method 12f are oils for external use produced with 1 part of the dried plants or parts of plants and 10 parts of vegetable oil, using the method given below. Groundnut oil, olive oil or sesame oil are normally used; other oils must be declared.

Combine 1 part of the minced drug with 10 parts of vegetable oil. Heat under CARBON DIOXIDE to approx. 37 °C and maintain at that temperature for 7 days; during that time, the mixture is stirred for 5 minutes every morning and evening, with the vessel kept closed. Express and filter.

LABELLING
Preparations made by Method 12f are labelled 'W 10%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12g: Liquid external applications
Preparations made by Method 12g are oils for external use produced with 1 part of the dried plants or parts of plants and 20 parts of vegetable oil, using the method

given below. Groundnut oil, olive oil or sesame oil are normally used; other oils must be declared.

Combine 1 part of the minced drug with 20 parts of vegetable oil. Heat under CARBON DIOXIDE to approx. 37,°C and maintain at that temperature for 7 days; during that time, the mixture is stirred for 5 minutes every morning and evening, with the vessel kept closed. Express and filter.

LABELLING
Preparations made by Method 12g are labelled 'W 5%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12h: Liquid external applications
Preparations made by Method 12h are oils for external use produced by mixing 1 part of an essential oil with 9 parts of vegetable oil. Groundnut oil, olive oil or sesame oil are normally used; other oils must be declared.

LABELLING
Preparations made by Method 12h are labelled '10%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12i: Liquid external applications
Preparations made by Method 12i are oils for external use produced by mixing 1 part of an essential oil with 19 parts of vegetable oil. Groundnut oil, olive oil or sesame oil are normally used; other oils must be declared.

LABELLING
Preparations made by Method 12i are labelled '5%'.

STORAGE
Protected from light, in sealed containers, as far as possible full ones.

Method 12j: Liquid external applications
Liquid external applications made by Method 12j are oily preparations for external use made from liquid dilutions.

To produce an oily dilution 3x, 1 part of liquid dilution 1x is succussed with 9 parts of anhydrous ethanol. 1 part of this dilution is treated in the same way to produce liquid dilution 3x. 1 part of liquid dilution 3x is mixed with 99 parts of vegetable oil.

The same method is used to produce oily dilution 4x from liquid dilution 2x, and oily dilutions from the 5x onwards. Olive oil is normally used; other oils must be declared.

LABELLING
Liquid external applications made by Method 12j are labelled 'oleos'.

Method 12k: Liquid external applications
Preparations made by Method 12k are tinctures for external use. They are made by the following method.

Fresh plants or parts of plants are finely minced. Loss on drying is determined on a sample. 1 part of plant material is immediately combined with three parts of water and heated to boiling for 30 minutes; water lost by evaporation is replaced. After this, 3.76 parts of water and 2.24 parts of ethanol 96 per cent are added. The additional amount of water required (W) is calculated as for Method 12c and added to the mixture. Leave to stand for not less than 5 days at a temperature not exceeding 20 °C; stir the mixture every morning and evening during those 5 days. Express and filter.

LABELLING
Liquid external applications made by Method 12k are labelled 'decoctum LE 10%'.

STORAGE
Protected from light.

Method 13: Ointments
Preparations made by Method 13 are made from one or more homoeopathic preparations in a suitable basis, usually wool alcohols ointment basis. Other bases must be declared.

Ointments must comply with the **Salben** monograph of the German Pharmacopoeia.

Not permitted are auxiliary substances such as antioxidants, stabilizers and—except in the case of hydrous gels and oil-in-water emulsions—preservatives.

LABELLING
Ointments containing the homoeopathic preparation in a ratio of 1 : 10 in the case of mother tinctures and decimal dilutions and of 1 : 100 in the case of centesimal dilutions are labelled with the homoeopathic preparation used.

Method 14: Suppositories
Preparations made by Method 14 are made from one or more homoeopathic preparations and a suitable basis. Hard fat is normally used as the basis; other bases must be declared.

Suppositories must comply with the requirements of the **Suppositorien** monograph in the German Pharmacopoeia. Additions other than the excipients listed under that heading in the *GHP* are not permitted.

'Uniformity of content' tests (V.5.2.2) are not required.

LABELLING
Suppositories containing the homoeopathic preparation in a ratio of 1 : 10 in the case of mother tinctures and decimal dilutions and of 1 : 100 in the case of centesimal dilutions are labelled with the homoeopathic preparation used.

Method 15: Eye drops

Eyes drops made by Method 15 are sterile aqueous fluids with a residual ethanol content of not more than one per cent.

They are produced from one or more homoeopathic preparations and comply with the requirements of the **Augentropfen** (eye drops) monograph in the German Pharmacopoeia.

They contain no additives except for preservatives and agents used to make the isotonic and adjust the pH.

To manufacture the eye drops, use water for injections or the solution of the isotonizing agent, normally sodium chloride, to produce the last two decimal dilutions and the last centesimal dilution respectively; other isotonizing agents must be declared. Ethanol-free drug vehicles may also be added.

LABELLING

State potency stages that have combined before being taken to higher potency stages; state drug vehicles if added.

Method 16: Mixtures

Preparations made by Method 16 are

1) Liquid and/or solid preparations in which the vehicle has been added in a proportion other than 1 to 10 or 1 to 100,
2) mixtures of liquid and/or solid preparations,
3) mixtures of liquid and/or solid preparations to which vehicles and/or auxiliary substances have been added.

All types of presentations may be produced from the above mixtures. Mixtures containing LIQUEUR WINE and/or preparations made by Method 46 must not be processed further.

Liquid external applications are manufactured as mixtures of preparations made by Methods 12a-i.

LABELLING

Composition is shown in such a way that the nature and amount of basic drug materials and of liquid and/or solid preparations incorporated in the mixture is clearly apparent. LIQUEUR WINE used in the production of vehicles must be declared on the container.

Method 17: LM potencies

To produce a LM I potency, dissolve 60 mg of a 3c trituration of the substance to be potentized in 20.0 ml of ethanol 15 per cent (= 500 drops). Transfer 1 drop of the solution to a small vial, add 2.5 ml of ethanol 86 per cent (= 100 drops) and shake vigorously 100 times. Moisten 100 g of size 1 granules (approx. 50,000 granules) evenly with the solution; following impregnation in a closed container the granules are air-dried. They represent the LM I potency.

To produce the LM II potency, transfer 1 granule of the LM I potency to a small vial and dissolve in 1 drop of water; add 2.5 ml of ethanol 86 per cent (= 100 drops) and shake vigorously 100 times. Moisten 100 g size 1 granules (approx. 50,000 granules) evenly with the solution; following impregnation in a closed container

the granules are air-dried.

Higher potencies are produced by the same method.

To produce liquid LM potencies, dissolve 1 granule of the required potency in 10.0 ml of ethanol 15 per cent. The solution is the same potency as the granule dissolved in it.

Method 18a: Heat-treated mother tinctures and liquid dilutions of these

Mother tinctures made by Method 18a are produced like mother tinctures made by Method 2a and heat-treated.

The mixture containing the total amount of ethanol 86 per cent required is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is processed as under Method 2a.

Potentization

The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 43 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 30 per cent.
The 3rd decimal dilution (3x) is made with
1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING

Preparations made by Method 18a are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 18b: Heat-treated mother tinctures and liquid dilutions of these

Mother tinctures made by Method 18b are produced like mother tinctures made by Method 2b and heat-treated.

The mixture containing the total amount of ethanol 62 per cent required is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is processed as under Method 2a. Use ethanol 30 per cent to adjust to any value required by the Monograph.

Potentization

The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 30 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 18b are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 18c: Heat-treated mother tinctures and liquid dilutions of these
Mother tinctures made by Method 18c are produced like mother tinctures made by Method 3a and heat-treated.

The mixture containing the total amount of ethanol 86 per cent required is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is processed as under Method 2a. Use ethanol 62 per cent to adjust to any value required by the Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 62 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 43 per cent.
The 3rd decimal dilution (3x) is made with
1 part of the 2nd decimal dilution and
9 parts of ethanol 30 per cent,
The 4th decimal dilution (4x) is made with
1 part of the 3rd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 18c are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 18d: Heat-treated mother tinctures and liquid dilutions of these
Mother tinctures made by Method 18d are produced like mother tinctures made by Method 3b and heat-treated.

The mixture containing the total amount of ethanol 73 per cent required is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is processed as under Method 2a. Use ethanol 43 per cent to adjust to any value required by Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 43 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 30 per cent.
The 3rd decimal dilution (3x) is made with

1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 18d are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 18e: Heat-treated mother tinctures and liquid dilutions of these
Mother tinctures made by Method 18e are produced like mother tinctures made by Method 3c and heat-treated.

The mixture containing the total amount of ethanol 43 per cent required is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is processed as under Method 2a. Use ethanol 30 per cent to adjust to any value required by Monograph.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 30 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 18e are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 18f: Heat-treated mother tinctures and liquid dilutions of these
Mother tinctures made by Method 18f are produced like mother tinctures made by Method 4a and heat-treated.

The mixture containing the total amount of ethanol 43 in the given concentration is heated to 37 °C in a covered container and maintained at that temperature for one hour, stirring occasionally. After cooling the mixture is macerated as per the TINCTURES Monograph in the Pharmacopoeia and then processed as under Method 4a.

Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).
the 2nd decimal dilution (2x) is made with
1 part of the mother tincture
9 parts of ethanol of the same concentration.

Subsequent decimal dilutions are produced in the same way, reducing the ethanol concentration stage by stage in the sequence 94 - 86 - 73 - 62 - 43 - 30 - 15 per cent until an ethanol concentration of 15 per cent is reached.

LABELLING
Preparations made by Method 18f are labelled 'ethanol. digested'; the same applies to presentations made from them.

Method 19a: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19a are produced by maceration using the procedure given below.

Prepare the mixture as per Method 2a, adding the total amount of ethanol 86 per cent required. Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph by the method given under Method 1.

Potentization
The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 43 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 30 per cent.
The 3rd decimal dilution (3x) is made with
1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 19a are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 19b: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19b are produced by maceration using the procedure given below.

Prepare the mixture as per Method 2b, adding the total amount of ethanol 62 per cent required. Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph using ethanol 30 per cent.

Potentization
The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of ethanol 30 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and

9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 19b are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 19c: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19c are produced by maceration using the procedure given below.

Prepare the mixture as per Method 3a, adding the total amount of ethanol 86 per cent required. Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph using ethanol 62 per cent.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 62 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 43 per cent.
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol 30 per cent,
the 4th decimal dilution (4x) with
1 part of the 3rd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 19c are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 19d: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19d are produced by maceration using the procedure given below.

Prepare the mixture as per Method 3b, adding the total amount of ethanol 73 per cent required. Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph using ethanol 43 per cent.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 43 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 30 per cent,
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 19d are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 19e: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19e are produced by maceration using the procedure given below.

Prepare the mixture as per Method 3c, adding the total amount of ethanol 43 per cent required. Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph using ethanol 30 per cent.

Potentization
The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of ethanol 30 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 19e are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 19f: Heat-treated mother tinctures and liquid preparations made from these
Mother tinctures made by Method 19f are produced by maceration using the procedure given below.

Prepare the mixture as per Method 4a, adding the total amount of ethanol in the required concentration: Heat under reflux to boiling and maintain at boiling temperature for 30 minutes. Allow to cool and leave to stand in a closed container for 24 hours; express and filter.

Adjust to any value given in the Monograph by the method given under Method 4a.

Potentization

The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).

The 2nd decimal dilution (2x) is made with

1 part of the mother tincture and

9 parts of ethanol of the same concentration.

Subsequent dilutions are produced in the same way, reducing the ethanol concentration stage by stage in the sequence 94 - 86 - 73 - 62 - 43 - 30 - 15 per cent until an ethanol concentration of 15 per cent is reached.

LABELLING

Preparations made by Method 19f are labelled 'ethanol. decoct.'; the same applies to presentations made from them.

Method 20: Heat-treated mother tinctures and liquid dilutions made from these Mother tinctures made by Method 20 are produced from dried plants or parts of plants, using 1 part of the plant drug to 10 parts of ethanol of a suitable concentration and following the procedure given below. The quantities of ethanol and water required to achieve the prescribed concentration are added separately.

Add the total amount of ethanol to the minced plant drug (710 μm), cover, and leave to stand for 15 minutes. Add the water, heated to boiling, and keep the mixture at boiling point under reflux for 5 minutes. Allow to cool and then leave to stand in a closed container for 24 hours; express and filter.

Potentization

The mother tincture is equivalent to the 1st decimal dilution (ø = 1x)

The 2nd decimal dilution (2x) is made with

1 part of the mother tincture

9 parts of ethanol of the same concentration.

Subsequent dilutions are produced in the same way, reducing the ethanol concentration stage by stage in the sequence 94 - 86 - 73 - 62 - 43 - 30 - 15 per cent until an ethanol concentration of 15 per cent is reached.

LABELLING

Preparations made by Method 20 are labelled 'ethanol. infusion'; the same applies to presentations made from them.

Method 21: Rh mother tinctures and liquid dilutions made from these Rh mother tinctures made by Method 21 are produced from fresh plants that yield at least 50 per cent of expressed fluid; no vehicle is added.

The plants are minced and expressed immediately on harvesting. The expressed fluid is transferred to containers that are no more than one quarter full and exposed to the diurnal temperature changes ('Rh') described below.

In the morning, bring the expressed fluid to a temperature of approx. 37 °C over a period of at least 30 minutes and maintain at this temperature until evening, when the temperature is reduced to approx. 4 °C over a period of at least 30

minutes; the fluid is maintained at that temperature over night.
Shake the container for at least 10 minutes during each temperature phase.
Filter as soon as fermentation has ceased.

Potentization
The first decimal dilution (1x) is made with
1 part of the Rh mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way; 'Water for Injections' is the vehicle used for all dilutions.
Transfer the dilutions immediately to containers with a maximum capacity of 20 ml. Heat to 70 °C and maintain at that temperature for 1 hour on three consecutive days, maintaining them at room temperature in the interim periods.

LABELLING
Preparations made by Method 21 are labelled 'Rh'; the same applies to presentations made from them.

STORAGE
Rh mother tinctures are stored in tightly sealed containers and protected from light.

Method 22: Rh mother tinctures and liquid dilutions made from these
Rh mother tinctures made by Method 22 are produced from fresh plants that yield less than 50 per cent of expressed fluid; no vehicle is added.
The plants are minced immediately on harvesting. The minced plant material is exposed to the diurnal temperature change ('Rh') which is described under Method 21 for approx. 10 days and then expressed.
The expressed fluid is treated as per Method 21 until fermentation is complete.
Filter as soon as fermentation has ceased.

Potentization
The first decimal dilution (1x) is made with
1 part of the Rh mother tincture and
9 parts of water for injections.
Proceed in the same manner for subsequent dilutions; 'Water for Injections' is the vehicle used for all dilutions.
Transfer the dilutions immediately to containers with a maximum capacity of 20 ml. Heat to 70 °C and maintain at that temperature for 1 hour on three consecutive days, maintaining them at room temperature in the interim periods.

LABELLING
Preparations made by Method 22 are labelled 'Rh'; the same applies to presentations made from them.

STORAGE
Rh mother tinctures are stored in tightly sealed containers and protected from

light.

Method 23: Heat-treated aqueous mother tinctures and liquid dilutions made from these.

Aqueous mother tinctures made by Method 23 are produced from 1 part of minced plant drug and 10 parts of water, following the procedure given below.

Combine 1 part of the minced plant drug with 10 parts of water at a temperature of over 90 °C, place on a water bath and maintain at that temperature for 30 minutes, stirring repeatedly. Filter hot. If gentle pressure applied to the drug residue does not achieve a final weight of mother tincture equal to 10 parts, pour a sufficient amount of boiling water over the drug residue and express gently. Use the resulting extract to make up the final weight.

Potentization

The mother tincture is equivalent to the 1st decimal dilution (ø= 1x)

The 2nd decimal dilution (2x) is made with

1 part of the mother tincture and

9 parts of water for injections.

Proceed in the same manner for subsequent dilutions.

Aqueous mother tinctures made by Method 23 are normally processed immediately; they are used exclusively to produce 'Liquid dilutions for injection' by Method 11 and 'Eye drops' by Method 15, or in mixtures according to Method 16.

Aqueous mother tinctures made by Method 23 and their liquid dilutions must comply with the 'Test for sterility' of the German Pharmacopoeia if stored for further processing.

LABELLING

Preparations made by Method 23 are labelled 'Decoct.'; the same applies to presentations made from them.

Method 23b: Heat-treated aqueous mother tinctures and liquid dilutions made from these.

Aqueous other tinctures made by Method 23b are made from fresh plants or parts of plants by the method given below.

Before processing the plant material, determine loss on drying on a sample. Calculate the amount of water (W) required with the aid of the following formula:

$$W = \frac{M \cdot (300 - D)}{100} \text{ [kg]}$$

M = weight of plant material in kg

D = loss on drying in per cent

Heat the calculated amount of water to a temperature of over 90 °C and add the minced plant material. Maintain at that temperature for 30 minutes under reflux, stirring repeatedly. Express and filter.

The 1st decimal dilution (1x) is made with
3 parts of the mother tincture and
7 parts of water for injections,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

Aqueous mother tinctures made by Method 23b are normally processed immediately; they are used exclusively to produce 'Liquid dilutions for injection' by Method 11 and 'Eye drops' by Method 15.

Aqueous mother tinctures made by Method 23b and their liquid dilutions must comply with the 'Test for sterility' of the German Pharmacopoeia if stored for further processing.

LABELLING
Preparations made by Method 23b are labelled 'Decoct.'; the same applies to presentations made from them.

Method 24: Heat-treated aqueous mother tinctures and liquid dilutions made from these
Aqueous mother tinctures made by Method 24 are produced from 1 part of minced plant drug and 10 parts of water, following the procedure given below.

Combine 1 part of the minced plant drug in a mortar with 3 - 5 times the amount of water, knead through a number of times and leave to stand for 15 minutes. After this period add the remaining water which has been heated to boiling. Place the mixture on a water bath and maintain at a temperature of more than 90 °C for 5 minutes, stirring repeatedly. Cover and leave to stand until cold. If gentle pressure on the drug residue does not achieve a final weight of 10 parts of mother tincture, pour a sufficient amount of boiling water over the drug residue and express gently. Use the resulting extract to make up the final weight.

Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x)
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

Aqueous mother tinctures made by Method 24 are normally processed immediately; they are used exclusively to produce 'Liquid dilutions for injection' by Method 11 and 'Eye drops' by Method 15, or in mixtures according to Method 16.

Aqueous mother tinctures made by Method 24 and their liquid dilutions must comply with the 'Test for sterility' of the German Pharmacopoeia if stored for further processing.

LABELLING
Preparations made by Method 24 are labelled 'Decoct.'; the same applies to

presentations made from them.

Method 24b: Heat-treated aqueous mother tinctures and liquid dilutions made from these

Aqueous other tinctures made by Method 24b are made from fresh plants or parts of plants by the method given below.

Before processing the plant material, determine loss on drying on a sample. Calculate the amount of water (W) required with the aid of the following formula:

$$W = \frac{M \cdot (400 - D)}{100} \text{ [kg]}$$

M = weight of plant material in kg

D = loss on drying in per cent

Heat the minced plant material and the calculated amount of water to a temperature of 37 °C and maintain at that temperature for 1 hour, stirring occasionally. Express and filter.

The 1st decimal dilution (1x) is made with

4 parts of the mother tincture and

6 parts of water for injections,

the 2nd decimal dilution (2x) with

1 part of the 1st decimal dilution and

9 parts of water for injections.

Subsequent dilutions are produced in the same way.

Aqueous mother tinctures made by Method 24b are normally processed immediately; they are used exclusively to produce 'Liquid dilutions for injection' by Method 11.

Aqueous mother tinctures made by Method 24b and their liquid dilutions must comply with the 'Test for sterility' of the German Pharmacopoeia if stored for further processing.

LABELLING

Preparations made by Method 24b are labelled 'Decoct.'; the same applies to presentations made from them.

Method 25: Zimpel's spagyric mother tinctures and preparations made from these

Spagyric mother tinctures made by Method 25 are produced from fresh plants or parts of plants, following the procedure given below.

Finely mince the plants or parts of plants. Using a suitable container, combine 1 part of the plant material with 1 part of water and 0.005 parts of yeast; leave to ferment at 20 - 25 °C, stirring the mixture once a day. As soon as fermentation ceases, steam distil the material into a collecting vessel containing 0.4 parts of ethanol 86 per cent per 1 part of plant material. Terminate distillation when the mixture of ethanol and distillate in the collecting vessel is two parts to one part of plant material.

Dry the expressed residue and incinerate at approx. 400 °C. Add the residue to

the distillate; filter after 48 hours.

Potentization
The 1st decimal dilution (1x) is made with
2 parts of the mother tincture and
8 parts of a mixture of 2 parts of ethanol 30 per cent and 1 part of water,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of a mixture of 2 parts of ethanol 30 per cent and 1 part of water.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 25 are labelled 'spag. Zimpel'; the same applies to presentations made from them.

Method 26: Zimpel's spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 26 are produced from dried plants or parts of plants, following the procedure given below.

In a suitable container, combine 1 part of the minced plant material (8,000 μm) with 3 parts of water and 0.01 parts of yeast; leave to ferment at 20 - 25 °C, stirring the mixture once a day. As soon as fermentation ceases, steam distil the material into a collecting vessel containing 2 parts of ethanol 86 per cent per 1 part of plant material. Terminate distillation when the mixture of ethanol and distillate in the collecting vessel is 10 parts to 1 part of plant material.

Dry the expressed residue and incinerate at approx. 400 °C. Add the residue to the distillate; filter after 48 hours.

Potentization
The mother tincture is equivalent to the first decimal dilution (ø = 1x).
The second decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of a mixture of 2 parts of ethanol 30 per cent and 1 part of water.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 26 are labelled 'spag. Zimpel'; the same applies to presentations made from them.

Method 27: Krauss' spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 27 are produced from fresh plants or parts of plants containing more than 70 per cent of moisture (loss on drying), following the procedure given below.

Finely mince the plant material and store in a cool place. Determine loss on drying on a sample. In a suitable container, combine the plant material with water, sucrose and yeast; calculate the amount of water required (W) according to the formula:

$$W = \frac{M \cdot D}{100} \text{ [kg]}$$

the amount of sucrose required (S) according to the formula:

$$S = 2 \cdot M \cdot D \text{ [g]}$$

the amount of yeast required (Y) according to the formula:

$$Y = 0.1 \cdot M \cdot D \text{ [g]}$$

M = mass of plant material in kg
D =loss on drying in sample in per cent.

Close the container with a fermentation lock and leave the mass to ferment at a temperature of approx. 35 °C. As soon as fermentation has ceased, express. Determine the ethanol concentration and adjust with ethanol 96 per cent or water to a 15 per cent (m/m) ethanol concentration. Store protected from light and at a temperature not exceeding 20 °C (extract A).

Air-dry the plant residue and percolate with ethanol 86 per cent by the method given in the German Pharmacopoeia under **Extrakte**; calculate the amount of ethanol 86 per cent required (E) according to the formula

$$E = \frac{M \cdot D}{100} \text{ [kg]}$$

M = mass of fresh plant material in kg
D = loss on drying in sample in per cent.
(Extract B).

Potentize Extract A) and Extract B) separately and produce the mother tincture and dilutions of it in the same way as for Method 27.

Potentization of Extract A)
The 1st decimal dilution (1x) is made with
2 parts of Extract A) and
8 parts of ethanol 15 per cent.

Potentization of Extract B)
The 1st decimal dilution (1x) is made with
1 part of Extract B) and
9 parts of ethanol 86 per cent,
the 2nd decimal dilution (2x) with
1 part of the 1st decimal dilution (1x) and
9 parts of ethanol 86 per cent.
The mother tincture (3x) is made with
1 part of the 2nd decimal dilution (2x) of Extract A),

1 part of the 2nd decimal dilution (2x) of Extract B) and
8 parts of ethanol 30 per cent.
Filter if required.
The 4th decimal dilution (4x) is made with
1 part of the mother tincture (3x) and
9 parts of ethanol 30 per cent.
Subsequent dilutions are produced in the same way.

LABELLING
Preparations made by Method 27 are labelled 'spag. Krauss'; the same applies to presentations made from them.

Method 28: Krauss' spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 28 are produced from fresh plants or parts of plants containing not less than 40 and not more than 70 per cent of moisture (loss on drying), following the procedure given with Method 27.

Unlike with Method 27, calculate the amount of water required (W) according to the formula:

$$W = \frac{2 \cdot M \cdot D}{100} \text{ [kg]}$$

the amount of sucrose required (S) according to the formula:

$$S = 3 \cdot M \cdot D \text{ [g]}$$

the amount of yeast required (Y) according to the formula:

$$Y = 0.15 \cdot M \cdot D \text{ [g]}$$

the amount of ethanol 86 per cent (E) required for percolation according to the formula in Method 27.

M = mass of fresh plant material in kg
D = loss on drying in sample in per cent.

Continue to potentize Extract A) and produce potencies of Extract B) separately to the 2nd decimal dilution (2x) and combine to produce the mother tincture (3x).

Potentization of Extract A)
The 1st decimal dilution (1x) is made with
3 parts of Extract A) and
7 parts of ethanol 15 per cent.

Potentize Extract A) and Extract B) and produce the mother tincture and dilutions of it in the same way as for Method 27.

LABELLING Preparations made by Method 28 are labelled 'spag. Krauss'; the same applies to presentations made from them.

Method 29: Krauss' spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 29 are produced from fresh plants or parts of plants containing not more than 40 per cent of moisture (loss on drying), following the procedure given with Method 27.

Unlike with Method 27, calculate the amount of water required (W) according to the formula:

$$W = \frac{3 \cdot M \cdot D}{100} \text{ [kg]}$$

the amount of sucrose required (S) according to the formula:

$$S = 4 \cdot M \cdot D \text{ [g]}$$

the amount of yeast required (Y) according to the formula:

$$Y = 0.2 \cdot M \cdot D \text{ [g]}$$

the amount of ethanol 86 per cent (E) required for percolation according to the following formula:

$$E = \frac{2 \cdot M \cdot D}{100} \text{ [kg]}$$

M = mass of fresh plant material in kg
D = loss on drying in sample in per cent.

Potentize Extract A) and Extract B) separately to the 2nd decimal dilution (2x) and combine to produce the mother tincture (3x).

Potentization of Extract A)
The 1st decimal dilution (1x) is made with
4 parts of Extract A) and
6 parts of ethanol 15 per cent.

Continue to potentize Extract A) and produce potencies of Extract B) and produce the mother tincture and dilutions of it in the same way as for Method 27.

Potentization of Extract B)
The 1st decimal dilution (1x) is made with
2 parts of Extract B) and
8 parts of ethanol 86 per cent,

Potentize Extract A) and Extract B) and produce the mother tincture and dilutions of it in the same way as for Method 27.

LABELLING
Preparations made by Method 29 are labelled 'spag. Krauss'; the same applies to presentations made from them.

Method 30: Krauss' spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 30 are produced from dried plants or parts of plants, following the procedure given with Method 27.

Unlike with Method 27, the aqueous mixture consists of 100 parts of powdered plant drug (710 µm), 400 parts of water, 40 parts of sucrose and 2 parts of yeast. The expressed plant residue is percolated with 4 parts of ethanol 86 per cent to 1 part of air-dried residue.

Extract A) and Extract B) are equivalent to the 1st decimal dilution (1x). Potentize separately to the 2nd decimal dilution (2x) and combine to produce the mother tincture (3x). Potentize Extract A) and Extract B) according to Method 27. The mother tincture (3x) is made with

0.5 parts of the 2nd decimal dilution (2x) of Extract A),
0.5 parts of the end decimal dilution (2x) of Extract B) and
9 parts of ethanol 30 per cent.

Filter if required.

Potentize the mother tincture (3x) according to Method 27.

LABELLING

Preparations made by Method 30 are labelled 'spag. Krauss'; the same applies to presentations made from them.

Method 31: Spagyric mother tinctures and preparations made from these Spagyric mother tinctures made by Method 31 are produced from fresh plants or parts of plants, following the procedure given below.

Mince the plants or parts of plants very finely. In a suitable container, combine 100 parts of plant material with 200 parts of water and 0.05 parts of yeast. Leave to ferment at a temperature of 18 °C, stirring the mixture daily. As soon as fermentation has ceased, adjust to an ethanol content of between 10.0 and 15.0 per cent, using ethanol 86 per cent; the ethanol resulting from fermentation is taken into account.

Distil at a pressure of 3.2 bar, using suitable apparatus. Dry the residue and incinerate at a temperature above 700 °C; let the ash cool down to approx. 150 °C and combine with the distillate.

Distil the resulting mixture at normal pressure. Dry the residue and incinerate at a temperature above 850 °C. Let the ash cool and combine with the distillate. 24 hours after adding the ash stir the mixture thoroughly; filter after another 60 hours. The filtrate represents the mother tincture.

Potentization

The first decimal dilution (1x) is made with

1 part of the mother tincture and
9 parts of a mixture of 1 part of ethanol 86 per cent and 4 parts of isotonic saline.

Subsequent dilutions are produced in the same way.

LABELLING

Preparations made by Method 31 are labelled 'spag. bidest.'; the same applies to presentations made from them.

Method 32: Buffered aqueous mother tinctures and liquid dilutions made from them

Buffered aqueous mother tinctures made by Method 32 are produced by macerating fresh plants or parts of plants, using the procedure given below.

Before the material is processed, take a sample and determine loss on drying. To 1 part of the plant material add 2 parts of ascorbate phosphate buffer solution and reduce the mixture to a homogenous slurry.

Calculate the total amount of ascorbate phosphate buffer solution (B) required according to the following formula, subtract the amount already used and add the remainder to the mixture.

$$B = \frac{4 \cdot M \cdot D}{100} \text{ [kg]} \qquad (3)$$

M = weight of the plant material in kg
D = loss on drying in the sample in per cent
Express and filter after not more than 60 minutes.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
1 part of ascorbate phosphate buffer solution,
the second decimal dilution (2x) with
1 part of the 1st decimal dilution and
9 parts of ascorbate phosphate buffer solution.

Subsequent dilutions are produced by the same method. Up to and including the 5th decimal dilution potentize with ascorbate phosphate buffer solution, from the 6th decimal solution onwards with isotonic saline.

With mother tinctures and liquid dilutions with high frothing potential potentization differs from the usual method; in containers filled so that there are no bubbles, potentize by mixing for not less than 1 minute in a device that produces rotary, tipping or rocking movements in constantly alternating acceleration and deceleration.

Buffered aqueous mother tinctures made by Method 32 are processed immediately. They are exclusively intended for the manufacture of 'Liquid dilutions for injection' by Method 11.

Liquid dilutions prepared by Method 32 must comply with the 'Test for Sterility' of the German Pharmacopoeia if stored for further processing.

LABELLING

Preparations made by Method 32 are labelled 'col.'; the same applies to presentations made from them.

Method 33a: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 33a are produced by macerating and

fermenting fresh plants or parts of plants, using the procedure given below.

Combine 100 parts of finely minced plant material with 0.75 parts of honey, 0.75 parts of lactose and 50 parts of water; determine the pH of the mixture. Every morning and evening place the mixture for a two-hour period in a mixture of ice and water; stir well before and after this. At all other times maintain on a water bath at approx. 37 °C. As soon as the pH begins to drop, maintain the mixture at room temperature, except for the two two-hour cooling periods per day. Unless otherwise stated in the Monograph, express after 3 1/2 days during one of the cooling phases. Continue to place the expressed liquid in a mixture of ice and water every morning and evening for 3 1/2 days; stir well immediately before and after doing so. For the rest of the time keep at room temperature. After 3 1/2 days filter the liquid through muslin; the filtrate is naturally cloudy.

Incinerate an adequate amount of the air-dried expressed plant residue in a porcelain crucible at a temperature where it turns a dark red. Immediately after filtration, add approx. 50 mg of ash per 100 ml of the filtrate. This mixture represents the mother tincture.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with

1 part of the mother tincture and

9 parts of a mixture of 1 part of ethanol 86 per cent and 4 parts of isotonic saline.

Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with

1 part of the mother tincture and

99 parts of water for injections.

Liquid dilutions made by Method 33a must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 33a are labelled 'ferm 33a'; the same applies to presentations made from them.

STORAGE

Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 33b: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 33b are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.

Method 33b differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 0.75 parts of honey, 0.75 parts of lactose and 75 parts of water.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization
The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.
The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 33b must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 33b are labelled 'ferm 33b'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 33c: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them
Aqueous mother tinctures made by Method 33c are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.
Method 33c differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 0.75 parts of honey, 0.75 parts of lactose and 125 parts of water.
Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization
The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.
The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 33c must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 33c are labelled 'ferm 33c'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 33d: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 33d are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.

Method 33d differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 0.75 parts of honey, 0.75 parts of lactose and 200 parts of water.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first vicesimal dilution (H) is made with
1 part of the mother tincture and
19 parts of water for injections.

Subsequent dilutions are produced in the same way. They are designated as follows: 2nd dilution as G, 3rd dilution as F, 4th dilution as E, 5th dilution as D, 6th dilution as C, 8th dilution as B and 10th dilution as A.

Liquid dilutions made by Method 33d must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 33d are labelled 'ferm 33d'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 33e: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 33e are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.

Method 33e differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 0.75 parts of honey, 0.75 parts of lactose and 275 parts of water.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization
The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.
The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 33e must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 33e are labelled 'ferm 33e'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 34a: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them
Aqueous mother tinctures made by Method 34a are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.
Method 34a differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material and 50 parts of whey.
Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization
The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.
The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 34a must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 34a are labelled 'ferm 34a'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 34b: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 34b are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.

Method 34b differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 25 parts of water and 50 parts of whey.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 34b must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 34b are labelled 'ferm 34b'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 34c: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 34c are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.

Method 34c differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 75 parts of water and 50 parts of whey.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 34c must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 34c are labelled 'ferm 34c'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 34d: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them
Aqueous mother tinctures made by Method 34d are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under Method 33a.
Method 34d differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 110 parts of water and 15 parts of whey.
Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization
The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.
The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.
Liquid dilutions made by Method 34d must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING
Preparations made by Method 34d are labelled 'ferm 34d'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 34e: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them
Aqueous mother tinctures made by Method 34e are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given under

Method 33a.

Method 34e differs from Method 33a in that the mixture is made up with 100 parts of finely minced plant material, 225 parts of water and 50 parts of whey.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with

1 part of the mother tincture and

9 parts of water for injections.

Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with

1 part of the mother tincture and

99 parts of water for injections.

Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 34e must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 34e are labelled 'ferm 34e'; the same applies to presentations made from them.

STORAGE

Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 35a: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them

Aqueous mother tinctures made by Method 35a are produced by macerating and fermenting fresh plants or parts of plants, using the procedure given below.

Divide 100 parts of finely minced plant material into 7 portions. In the morning, combine 1 portion of the finely minced plant material with 0.75 parts of honey and 500 parts of water; determine the pH of the mixture. Place the mixture in a water bath at about 37 °C. In the evening, place the mixture for a two-hour period In a mixture of ice and water; stir well immediately before and after this. Return the mixture to the water bath at approx. 37 °C. Express the mixture 24 hours after first preparing it and determine the pH of the liquid.

Add another portion of the finely minced plant material to the extract and in the evening place for 2 hours in a mixture of ice and water; stir immediately before and after this. If the pH has not changed, keep the mixture of a water bath at about 37 °C for the remaining time; if the pH has decreased, keep the mixture at room temperature. Express 24 hours after first making the mixture and determine the pH of the liquid.

Proceed in the same way with the 5 remaining portions of plant material over the next 5 days. Leave the final liquid to stand for some hours before filtering through muslin; the filtrate is naturally turbid.

Incinerate an adequate amount of the air-dried expressed plant residue in a porcelain crucible at a temperature where it turns a dark red. Immediately after

filtration, add approx. 50 mg of ash per 100 ml of the filtrate. This mixture represents the mother tincture.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with

1 part of the mother tincture and

9 parts of water for injections.

Prepare subsequent dilutions in the same way.

The first decimal dilution (1c) is made with

1 part of the mother tincture and

99 parts of water for injections.

Prepare subsequent dilutions in the same way.

Liquid dilutions made by Method 35a must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 35a are labelled 'ferm 35a'; the same applies to presentations made from them.

STORAGE

Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 35b: Heat-treated and fermented aqueous mother tinctures and liquid dilutions made from them.

Aqueous mother tinctures made by Method 35b are produced by macerating and fermenting dried plants, parts of plants or plant secretions, using the procedure given under Method 35a.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with

1 part of the mother tincture and

9 parts of water for injections.

Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with

1 part of the mother tincture and

99 parts of water for injections.

Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 35b must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 35b are labelled 'ferm 35b'; the same applies to presentations made from them.

STORAGE
Protected from light, in tightly sealed containers; the mother tincture below 15 °C.

Method 36: Heat-treated and fermented aqueous mother tinctures and liquid dilutions of these

Aqueous mother tinctures made by Method 36 are produced by macerating and fermenting dried plants or parts of plants or plant secretions, following the procedure given under Method 35a.

Method 36 differs from Method 35a in that the first mixture is made with the finely minced first portion of plant material, 300 parts of water and 200 parts of whey.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.

Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 36 must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before further processing.

LABELLING
Preparations made by Method 36 are labelled 'ferm 36'; the same applies to presentations made from them.

STORAGE
Protected from light, in well sealed containers; the mother tincture at below 15 °C.

Method 37a: Heat-treated and fermented aqueous mother tinctures and liquid dilutions of these

Aqueous mother tinctures made by Method 37a are produced by macerating and fermenting fresh plants or parts of plants, following the procedure given below.

Divide 100 parts of the plant material into 7 portions. The first mixture is made up in the morning, using one portion of the finely minced plant material, 0.15 parts of finely powdered haematite and 50 parts of water. Place the mixture on a water bath at approx. 37 °C. In the evening, place the mixture for 2 hours in a mixture of ice and water, stirring well before and after the 2-hour period. Replace on the water bath at approx. 37 °C. Express 24 hours after making up the mixture.

The next mixture is made up with the expressed liquid, another portion of finely minced plant material and 0.15 parts of finely powdered haematite and treated like the first mixture. Process the remaining 5 portions in the same way during the 5 days that follow. Leave the final expressed liquid to stand for a few

hours before filtering through muslin. The filtrate is naturally cloudy.

Incinerate an adequate amount of the air-dried plant residue in a porcelain crucible at a temperature where it turns a dark red. Immediately after filtration, add approx. 50 mg of ash per 100 ml of the filtrate. This mixture represents the mother tincture.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 37a must comply with the 'Test for sterility' in the German Pharmacopoeia if stored before further processing.

LABELLING

Preparations made by Method 37a are labelled 'ferm cum ferro'; the same applies to presentations made from them.

STORAGE

Protected from light, in well sealed containers; the mother tincture at below 15 °C.

Method 37b: Heat-treated and fermented aqueous mother tinctures and liquid dilutions of these

Aqueous mother tinctures made by Method 37b are produced by macerating and fermenting fresh plants or parts of plants, following the procedure given under Method 37a.

Method 37b differs from Method 37a in that the finely powdered haematite is replaced with the same amount of finely powdered zinc.

Wait not less than 6 months after adding the ash before processing the mother tincture. Discard any sediment that may have formed.

Potentization

The first decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of water for injections.
Subsequent dilutions are produced in the same way.

The first centesimal dilution (1c) is made with
1 part of the mother tincture and
99 parts of water for injections.
Subsequent dilutions are produced in the same way.

Liquid dilutions made by Method 37b must comply with the 'Test for sterility'

in the German Pharmacopoeia if stored before further processing.

LABELLING
Preparations made by Method 37b are labelled 'ferm cum zinco'; the same applies to presentations made from them.

STORAGE
Protected from light, in well sealed containers; the mother tincture at below 15 °C.

Method 38: Cold-treated aqueous mother tinctures and liquid dilutions made from them
Aqueous mother tinctures made by Method 38 are produced by macerating dried plants or parts of plants in the cold ('C'), following the procedure given below.

Combine the finely minced plant material with six times the amount (w/w) of a solution made with 8.8 parts of sodium chloride, 0.2 parts of sodium hydrogen carbonate and 991 parts of water. Store the mixture at a temperature of approx. 4 °C for 14 days, stirring well every morning and evening. Express. Store the expressed liquid at a temperature of approx. 4 °C and protected from light until the supernatant liquid is completely clear. The clear supernatant liquid represents the mother tincture. Process completely and immediately.

Potentization
The 1st vicesimal dilution (H) is made with
1 part of the mother tincture and
19 parts of water for injections.

Subsequent dilutions are produced in the same way and labelled as follows: 2nd dilution as G, 3rd dilution as F, 4th dilution as E, 5th dilution as D, 6th dilution as C, 8th dilution as B and 10th dilution as A.

Mother tinctures made by Method 38 are processed immediately. They are used exclusively for the manufacture of 'Liquid dilutions for injection' made by Method 11.

LABELLING
Preparations made by Method 38 are labelled 'C' ('K' in German); the same applies to presentations made from them.

Method 39a: Globuli velati (coated granules)
Preparations made by Method 39a are coated granules produced by the even application of a liquid preparation to size 5 sucrose granules (40-50 granules weigh 1 g).

To produce 100 parts of coated granules, combine 1 part of a preparation made by Methods 33-37 with 9 parts of sugar syrup and potentize by succussion; evenly apply these 10 parts to 100 minus x parts of sucrose granules, where x is the amount of sucrose in the sugar syrup.

LABELLING
Coated granules made by Method 39a are labelled to indicate the dilution stage of

the applied preparation.

Method 39b: Globuli velati (coated granules)
Preparations made by Method 39b are coated granules produced by the even application of a solid preparation to size 5 sucrose granules (40-50 granules weigh 1 g).

To produce 100 parts of coated granules, combine 1 part of a mixture of 10 parts of a trituration made by Method 6 and 20 parts of sugar syrup and apply evenly to 100 minus x minus y parts of sucrose granules, where x is the amount of sucrose in the sugar syrup and y is the amount of lactose in the incorporated trituration.

LABELLING
Coated granules made by Method 39b are labelled to indicate the dilution stage of the applied trituration.

Method 39c: Globuli velati (coated granules)
Preparations made by Method 39c are coated granules produced by the even application of a mixture made by Method 16, No. 3, to size 5 sucrose granules (40-50 granules weigh 1 g).

The mixture to be applied is produced with preparations made by Methods 6, 23, 24, 33a-e, 34-a-e, 35a-b, 36, 37a-b, 40b, and 40c and an adequate amount of sugar syrup. To produce 100 parts of Globuli velati, apply the mixture evenly to 100 minus x minus y parts of sucrose granules, where x is the amount of sucrose in the sugar syrup and y is the amount of lactose in the incorporated triturations.

LABELLING
Indicate the composition so that the type and amount of incorporated liquid and/or solid preparations are clearly apparent.

Method 40a: Potentized mixtures
Mixtures potentized by Method 40a may contain basic drug materials, solutions or triturations in combination with liquid preparations, liquid dilutions, and/mother tinctures which according to the Method of preparation are to be processed in a 1 : 10 ratio. Method 40a is limited to potentization of combined liquid preparations produced by Methods using a mixture of ethanol and water as the vehicle.

Potentization
Combine and succuss 1 part of the given mixture and 9 parts of ethanol in a suitable concentration for each potentizing stage.

Potentized mixtures may be used to produce all types of presentation. For 'Liquid dilutions for injection' made by Method 11 and 'Eye drops' made by Method 15, use the vehicle given in the Method for the final potentizing stage.

LABELLING
State the number of potentizing stages applied to the mixture; the same applies to presentations produced from potentized mixtures.

Method 40b: Potentized mixtures

Mixtures potentized by Method 40b may contain liquid preparations made by Methods 5b, 8b, 23, 24, 33a-e, 34a-e, 35a-b, 36, 37a-b, 41a-c and triturations made by Method 6.

Potentization

Combine and succuss 1 part of the given mixture and 9 parts of the vehicle for each potentizing stage. If the mixture contains preparations made by Methods 41a-c, use the vehicle given under those Methods for potentization. If mixtures potentized by Method 40b are used to produce Globuli velati, use sugar syrup as the vehicle for the final potentization stage; in all other cases use water for injections as the vehicle.

Mixtures potentized by Method 40b must comply with the 'Sterility test' in the German Pharmacopoeia if stored.

Potentized mixtures may be used to produce all types of presentation. For 'Liquid dilutions for injection' made by Method 11 and 'Eye drops' made by Method 15, use the vehicle given in the Method for the final potentizing stage.

LABELLING

State the number of potentizing stages applied to the mixture; the same applies to presentations produced from potentized mixtures.

Method 40c: Potentized mixtures

Mixtures potentized by Method 40c contain triturations made by Methods 6 and/or 7.

Potentization

Combine and triturate 1 part of the mixture and 9 parts of lactose for each potentizing stage, following the procedure given under Method 6.

Potentized mixtures may be used to produce all types of presentation.

LABELLING

State the number of potentizing stages applied to the mixture; the same applies to presentations produced from potentized mixtures.

Method 41a: Gl mother tinctures and liquid dilutions made from these

Gl mother tinctures made by Method 41a are produced by macerating animals, parts of animals or animal secretions with a glycerol solution (Gl) containing sodium chloride, following the procedure given below. Higher (warm-blooded) animals are processed immediately after slaughter. Lower animals are killed immediately before they are processed by gassing with CARBON DIOXIDE in a covered vessel.

Combine 1 part of finely minced animal material with 5 parts of a 1.5 per cent solution (w/w) of sodium chloride; after this add 95 parts of GLYCEROL. Store protected from light for not less than 7 days. Decant and if necessary filter through muslin. Bring any sediment present into suspension before processing the Gl mother tincture.

Potentization

The vehicle used for potentization is a solution of 0.2 part of sodium hydrogen carbonate and 8.8 parts of sodium chloride in 91 parts of WATER FOR INJECTIONS.

The Gl mother tincture is equivalent to the 2nd decimal dilution (ø = 2x) and the 1st centesimal dilution (ø = 1c).

The third decimal dilution (3x) is made with
1 part of the Gl mother tincture and
9 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

The second centesimal dilution (2c) is made with
1 part of the Gl mother tincture and
99 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

Gl mother tinctures made by Method 41a are used exclusively for the manufacture of preparations by Methods 7, 11, 13, 14, 15 and 39a-c, in mixtures made by Method 16, and in potentized mixtures made by Method 40b.

Liquid dilutions made by Method 41a must comply with the 'Test for sterility' in the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 41a are labelled 'Gl'; the same applies to presentations made from them.

Method 41b: Gl mother tinctures and liquid dilutions made from these

Gl mother tinctures made by Method 41b are produced by macerating animals, parts of animals or animal secretions with a glycerol solution (Gl) containing sodium chloride, following the procedure given below. Higher (warm-blooded) animals are processed immediately after slaughter. Lower animals are killed immediately before they are processed by gassing with CARBON DIOXIDE in a covered vessel.

Combine 1 part of finely minced animal material with 5 parts of a 4 per cent solution (w/w) of sodium chloride; after this add 95 parts of GLYCEROL. Store protected from light for not less than 7 days. Decant and if necessary filter through muslin. Bring any sediment present into suspension before processing the Gl mother tincture.

Potentization

The vehicle used for potentization is a solution of 0.2 part of sodium hydrogen carbonate and 8.8 parts of sodium chloride in 91 parts of WATER FOR INJECTIONS.

The Gl mother tincture is equivalent to the 2nd decimal dilution (ø = 2x) and the 1st centesimal dilution (ø = 1c).

The third decimal dilution (3x) is made with
1 part of the Gl mother tincture and
9 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

The second centesimal dilution (2c) is made with
1 part of the Gl mother tincture and

99 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

Gl mother tinctures made by Method 41b are used exclusively for the manufacture of preparations by Methods 7, 11, 13, 14, 15 and 39a-c, in mixtures made by Method 16, and in potentized mixtures made by Method 40b.

Liquid dilutions made by Method 41b must comply with the 'Test for sterility' in the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 41b are labelled 'Gl'; the same applies to presentations made from them.

Method 41c: Gl mother tinctures and liquid dilutions made from these

Gl mother tinctures made by Method 41c are produced by macerating animals, parts of animals or animal secretions with a glycerol solution (Gl) containing sodium chloride, following the procedure given below. Higher (warm-blooded) animals are processed immediately after slaughter. Lower animals are killed immediately before they are processed by gassing with CARBON DIOXIDE in a covered vessel.

Combine 1 part of finely minced animal material with 5 parts of an 8 per cent solution (w/w) of sodium chloride; after this add 95 parts of GLYCEROL. Store protected from light for not less than 7 days. Decant and if necessary filter through muslin. Bring any sediment present into suspension before processing the Gl mother tincture.

Potentization

The vehicle used for potentization is a solution of 0.2 part of sodium hydrogen carbonate and 8.8 parts of sodium chloride in 91 parts of WATER FOR INJECTIONS.

The Gl mother tincture is equivalent to the 2nd decimal dilution (ø = 2x) and the 1st centesimal dilution (ø = 1c).

The third decimal dilution (3x) is made with

1 part of the Gl mother tincture and

9 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

The second centesimal dilution (2c) is made with

1 part of the Gl mother tincture and

99 parts of the above vehicle.

Subsequent dilutions are produced in the same way.

Gl mother tinctures made by Method 41c are used exclusively for the manufacture of preparations by Methods 7, 11, 13, 14, 15 and 39a-c, in mixtures made by Method 16, and in potentized mixtures made by Method 40b.

Liquid dilutions made by Method 41c must comply with the 'Test for sterility' in the German Pharmacopoeia if stored before processing.

LABELLING

Preparations made by Method 41c are labelled 'Gl'; the same applies to presentations made from them.

Method 42: Mother tinctures and liquid dilutions
Mother tinctures made by Method 42 are made from freshly slaughtered animals or parts of these and a liquid vehicle. Disperse 1 part of finely minced animal material in 9 parts (= 1x) or 99 parts (= 1c or 2x) of glycerol 85 per cent and succuss. Filter if required.

Potentization
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture (1x) and
9 parts of glycerol 85 per cent,
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution or 1 part of the mother tincture (2x) and
9 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.
The 2nd centesimal dilution (2c) is made with
1 part of the mother tincture (1c) and
99 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.

Method 43: Mother tinctures and liquid dilutions
Mother tinctures made by Method 43 are made from animal or human organs or parts of organs that are subject to pathological changes. Disperse 1 part of minced starting material, which must comply with the 'Test for sterility' in the German Pharmacopoeia, in 10 parts of glycerol 85 per cent. Leave to stand for not less than 5 days before filtering.

Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol 30 per cent,
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol 43 per cent, unless another liquid vehicle is prescribed.
Subsequent dilutions are made in the same way.
The first centesimal dilution (1c) is made with
10 parts of the mother tincture and
90 parts of ethanol 30 per cent,
the 2nd centesimal dilution (2c) with
1 part of the 1st centesimal dilution (1c) and
99 parts of ethanol 43 per cent, unless another liquid vehicle is prescribed.
Subsequent dilutions are made in the same way.

Method 44: Mother tinctures and liquid dilutions
Mother tinctures made by Method 44 are made from killed cultures of microorganisms or from decomposition products of animal organs or from body fluids containing pathogens or pathological products. Combine and succuss 1 part

of the starting material—this must comply with the 'Test for sterility' in the German Pharmacopoeia—with 9 parts of glycerol 85 per cent. Leave to stand for not less than 5 days, then filter if required.

Unless otherwise stated in the Monograph, adjust cultures to 10^7 microorganisms per gram before sterilizing them.

Potentization

The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol 30 per cent,
the 3rd decimal dilution (3x) with
1 part of the 2nd decimal dilution and
9 parts of ethanol 43 per cent, unless another liquid vehicle is prescribed.
Subsequent dilutions are made in the same way.
The first centesimal dilution (1c) is made with
10 parts of the mother tincture and
90 parts of ethanol 30 per cent,
the 2nd centesimal dilution (2c) with
1 part of the 1st centesimal dilution (1c) and
99 parts of ethanol 43 per cent, unless another liquid vehicle is prescribed.
Subsequent dilutions are made in the same way.

Method 45: Nasal drops

Preparations made by Method 45 are aqueous liquids with a residual ethanol concentration of not more than one per cent.

They are made with one or more homoeopathic preparations and comply with the requirements of the **Nasentropfen** monograph in the German Pharmacopoeia.

Apart from auxiliaries used to preserve, increase viscosity, isotonize and adjust pH, no additives are permitted.

Potentize the last two decimal dilutions and the last centesimal dilution respectively with water for injections or the solution of isotonizing agent, usually sodium chloride; other isotonizing agents must be declared. Ethanol-free vehicles may also be added.

STORAGE

Protected from light.

LABELLING

Potency stages potentized to a higher level together must be stated, as must be the addition of drug vehicles.

Method 46: Liquid vinous dilutions

Preparations made by Method 46 are liquid decimal dilutions produced by potentizing liquid dilutions made by Methods 1, 2a, 3a, 4a, 5a or 8a through two potentizing stages with liqueur wine. Liquid dilutions made by Methods 1, 2a, 3a and 5a can only be potentized with liqueur wine from the 2nd decimal dilution (2x)

onwards; on the other hand all dilutions made by Method 8, including the 6x and 7x, may be potentized through two stages with liqueur wine using Method 46.

Liquid vinous dilutions made by Method 46 are processed immediately; they are intended exclusively for the manufacture of mixtures by Method 16.

LABELLING
Preparations made by Method 46 are labelled 'vinos'.

Method 47a: Pekana's spagyric mother tinctures and liquid dilutions of these Spagyric mother tinctures made by Method 47a are produced from fresh plants or parts of plants using the method given below.

Finely mince the plants or parts of plants. In a suitable container combine 1 part of plant material, 6 parts of water, 1 part of sucrose and 0.005 parts of yeast. Close the container with a fermentation lock and leave the mass to ferment at a temperature of approx. 20 - 25 °C. As soon as fermentation has ceased, decant the liquid part and express the plant residue. Adjust with ethanol 86 per cent or water to a 15 per cent ethanol concentration. Dry the plant residue and incinerate at about 900 °C. When the ash has cooled to about 20 °C, dissolve it in part of the ethanolic fraction and add to the total liquid. Filter after about 48 hours. This mixture is the mother tincture.

Potentization
The 1st decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.

LABELLING
Preparations made by Method 47a are labelled 'spag. Peka'; the same applies to presentations made from them.

Method 47b: Pekana's spagyric mother tinctures and liquid dilutions of these Spagyric mother tinctures made by Method 47b are produced from fresh plants or parts of plants using the method given as Method 47a.

Method 47b differs from Method 47a in that the powdered drug (710 µm) is mixed in cold water in a ratio of 1 : 6 and left to stand for 1 day. In a suitable container combine 1 part of the mixture with 1 part of sucrose and 0.005 parts of yeast. Ferment at a temperature of approx. 20 - 25 °C.

Potentization
The 1st decimal dilution (1x) is made with
1 part of the mother tincture and
9 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.

LABELLING
Preparations made by Method 47b are labelled 'spag. Peka'; the same applies to

presentations made from them.

Method 48: Ointments containing powdered metal
Ointments containing powdered metal produced by Method 48 contain powdered metal in an ointment base. They are exclusively produced for the manufacture of ointments by Method 13. Manufacture by mixing 1 part of the metal powder into 9 parts of ointment base. 80 per cent of the metal particles are less than 10 μm in diameter; no particle is larger than 50 μm.

Presentations made by Method 48 must comply with the Salben monograph in the German Pharmacopoeia.

LABELLING
Ointments containing powdered metal produced by Method 48 are labelled 'M'.

Method 49: Aqueous mother tinctures and liquid dilutions of these
Aqueous mother tinctures produced by Method 49 are made by macerating fresh plants or parts of plants by the following method.

Determine loss on drying and add the amount of water calculated as under Method 23b to the minced plant material. Express the plant material after not more than 2 hours and filter.

Potentize as for Method 23b.

Aqueous mother tinctures made by Method 49 are normally processed immediately. They are exclusively used to produce presentations by Method 11 and Method 15.

Aqueous mother tinctures made by Method 49 must comply with the 'Test for sterility' of the German Pharmacopoeia if stored before further processing.

LABELLING
Preparations made by Method 49 are labelled 'aquos'; the same applies to presentations made from them.

Method 50a: Strathmeyer's spagyric mother tinctures and liquid dilutions of these
Spagyric mother tinctures produced by Method 50a are made with dried plants or parts of plants or mixtures of dried plants or parts of plants and Strath yeast (*Candida utilis* cultivated with the drug extract specified in Methods 50a and 50b) by the method given below.

Put 5 parts of the minced drug in a suitable container and add 75 parts of water, 19 parts of sucrose and 1 part of yeast. Leave to ferment at 24 - 29 °C. After 3 days add 1 more part of yeast and leave to ferment for 3 more days. Express and process the drug extract immediately.

In a separate production process, macerate 25 parts of Strath yeast in 20 parts of ethanol for 5 days. Filter the yeast extract.

Combine 15 parts of yeast extract and 85 parts of drug extract and filter. To every 100 ml of the filtrate add 50 mg of ascorbic acid. This mixture is the mother tincture.

Potentization
Combine 2 parts of the mother tincture and 8 parts of ethanol 15 per cent and potentize. This yields the 2nd decimal dilution (2x).
The 3rd decimal dilution (3x) is made with
1 part of the 2nd decimal dilution and
9 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.

LABELLING
Preparations made by Method 50a are labelled 'spag. Strathmeyer'; the same applies to presentations made from them.

Method 50b: Strathmeyer's spagyric mother tinctures and liquid dilutions of these for the manufacture of Strathmeyer ointments
Spagyric mother tinctures produced by Method 50b are made with dried plants or parts of plants or mixtures of dried plants or parts of plants and Strath yeast (Candida utilis cultivated with the drug extract specified in Methods 50a and 50b) by the method given below.

Put 8 parts of the minced drug in a suitable container and add 74 parts of water, 14 parts of sucrose and 1 part of yeast. Leave to ferment at 24 - 29 °C for 6 days, express and filter. Store the drug extract at not more than 8 °C and protected from light for up to 6 weeks.

In a separate production process, macerate 25 parts of Strath yeast in 20 parts of ethanol for 5 days. Filter the yeast extract and evaporate to one tenth of the original mass under vacuum at a temperature not exceeding 40 °C.

Combine 1 parts of the concentrate and 99 parts of the drug extract. This mixture is the mother tincture.
Potentization
The mother tincture is equivalent to the 1st decimal dilution (ø = 1x).
The 2nd decimal dilution (2x) is made with
1 part of the mother tincture and
9 parts of ethanol 15 per cent.
Subsequent dilutions are made in the same way.

LABELLING
Preparations made by Method 50b are labelled 'spag. Strathmeyer'; the same applies to presentations made from them.

Method 50c: Strathmeyer ointments
Ointments produced by Method 50c are made from preparations produced by Method 50b and a base in a ratio of 1 : 3. The base consists of 4 parts of wool alcohols ointment and 1 part of lanolin.

The ointments comply with the **Salben** monograph of the German Pharmacopoeia.

Additives such as antioxidants, stabilizers and preservatives are not permitted.

Abies alba spag. Zimpel

Tips of non-woody fresh young twigs, with leaves and immature cones, of *Abies alba* Mill.

DESCRIPTION

The tips of twigs and cones have a resinous balsamic odour and slightly bitter, aromatic, resinous taste.

The young twigs are greyish or yellowy brown, not grooved, with fine or rough hairs but no glandular hairs. The stiff evergreen solitary leaves are spirally inserted on the stem but usually twisted at the base so that they form two lateral sets. Occasionally some of the leaves are obliquely erect on either side of the central line on the stem, creating a V-shaped channel. On vertical shoots, the flat leaves, 17 - 30 mm long and 2 - 3 mm wide, grow in all directions. The upper surface is grooved, dark shining green, with normally only a few short white lines at the tip. The underside is matt, with striking whitish or bluish white waxy bands on either side of the keel-like central vein. The tip of the leaf is blunt or emarginate, the margin flat. At the base the lamina narrows down to a short green petiole that is oval in cross section and attached to the shoot by a disc-like base. On removal of the leaf the disc comes away with the petiole, leaving a flat circular scar. Buds, which may be present at the tips of twigs, are not resinous, so that the scales are clearly visible. The buds of terminal shoots are occasionally slightly resinous at the base.

The erect green, bluish green or browny green cones are cylindrical, narrowing slightly towards the rounded tip. The central axis is covered with numerous densely imbricate bracts arranged in a spiral, with ovuliferous scales in their axils. The exserted bracts are linear and spatulate, dentate and with a long pointed process at the tip. They are narrower but longer than the ovuliferous scales. The part that forms the outside of the cone stands away horizontally or is reflexed. The ovuliferous scales have a cuneate base and are broadly rounded at the top; dorsum and margins are tomentose. Two unripe seeds with truncated cuneate wings sit near the base on the upper side.

PREPARATIONS

MANUFACTURE
The mother tincture and liquid dilutions by Method 25.

CHARACTERISTICS
The mother tincture is a pale yellow liquid with aromatic odour and taste.

IDENTIFICATION
Chromatography. Use thin-layer chromatography in a ready-made silica gel H *R* plate.

Test solution: To 10 ml of the mother tincture add 10 ml of saturated sodium chloride solution *RN* and extract three times, each time with 10 ml of pentane *R*. Dry the combined organic phases over anhydrous sodium sulphate *R*, filter and evaporate to about 0.5 ml on a water bath at about 30 °C.

Dissolve the residue in 1 ml of methanol *R*.

Control solution: Dissolve 5 mg each of borneol *R* and thymol *R* in 10 ml of methanol *R*.

Apply separately 10 µl of the test solution and 10 µl of the control solution. The mobile phase is a mixture of 7 parts by volume of ethyl acetate *R* and 93 parts by volume of toluene *R*. Allow the solvent front to rise 15 cm above the line of application. Following evaporation of the solvent spray the chromatograms with anisaldehyde reagent *R*, heat to 105 - 110 °C for 10 minutes and examine in daylight.

The chromatogram of the control solution has the yellowy green borneol zone in the lower and the red thymol zone in the middle third.

The chromatogram of the test solution has a reddish violet zone at the level of the borneol standard and several mauve and reddish violet zones between the borneol standard and the line of application; immediately above the borneol standard are a faintly mauve and a red zone, below the thymol standard a reddish violet and below the solvent front a bluish violet zone.

ASSAY FOR PURITY
Relative density (V.6.4): 0.968 - 0.978.

Dry residue (V.6.22.N2): Not less than 0.15 per cent.

STORAGE
Protected from light.